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TRANSACTIONS

OF THE

NATIONAL ASSOCIATION

FOR THE

STUDY OF PELLAGRA

SECOND TRIENNIAL MEETING

AT

COLUMBIA, SOUTH CAROLINA

OCTOBER 3 AND 4, 1912

THE R. L. BRYAN COMPANY
COLUMBIA, S. C.
1914

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Introductory Note

THE papers presented in this volume were read before the Second Triennial Meeting of the National Association for the Study of Pellagra. Other valuable papers were read also, but it has been impossible to obtain from the writers their manuscripts. Some of the papers by European contributors have not been corrected by their writers, for, although proof was sent to them, corrected copies have not been returned. To these contingencies is in part due the delay in publishing this report. For the next triennial meeting, to be held in 1915, the time and place have not been selected. The recognition of the presence of pellagra in almost every State in the Union and in most of the countries of the world gives reason to expect that the next meeting will be of international character.

Efforts made to amalgamate our organization with other societies have so far not succeeded, and it is hoped that a separate organization will continue to be maintained because of the great importance of the pellagra problem.

The cordial thanks of the association are due to The R. L. Bryan Printing Company, of Columbia, S. C., for assuming the financial responsibility of publishing these transactions.

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Resolutions

The following resolutions were adopted by the association:

Whereas, The second meeting of the National Association for the Study of Pellagra is about to close its most successful sessions at Columbia, it seems fitting before final adjournment that certain things should be made a matter of formal record; therefore, be it *resolved:*

1. That the association desires to express its appreciation of the courtesies exhibited by the city of Columbia, by the authorities of the Insane Asylum, and especially by its president, J. W. Babcock, to whose personal energy the success of this meeting has been largely due.

2. That this association reiterates the belief, formerly expressed, that the ultimate cause of pellagra is unknown, but it is the opinion that in view of the indictment against "spoiled corn" measures should be taken by proper enactment to prevent its sale and consumption as food.

3. That this association expresses the conviction that no satisfying evidence has ever been submitted which shows pellagra to be directly transmitted from man to man; and that in the present state of our knowledge the association regards measures of quarantine and isolation for the disease unnecessary and unwise.

4. That the association is convinced that there is at present no known specific remedy for pellagra, and any claim made for the efficacy of any especial therapeutic agent must be accepted with great caution.

5. That this association recognizes pellagra in the United States as a matter of great importance to the national public health and

notes with approval the interest of the United States Public Health Service in this subject. It is hoped the Congress of the United States may appropriate sufficient funds for the continued extension of the work.

6. The association wishes to record its appreciation of the benevolent and scientific spirit of Col. Robert M. Thompson, of New York, and Mr. J. H. McFadden, of Philadelphia, for endowing the Thompson-McFadden Pellagra Commission of the New York Post Graduate Medical School, which has been doing most excellent work in investigating pellagra in the South, and especially in Spartanburg, S. C.

Constitution

PREAMBLE.

Recognizing the necessity that has arisen demanding the further study of pellagra in the United States, and in order to preserve and protect the health of our people from a scourge that threatens to become national, the National Association for the Study of Pellagra hereby adopts the following Constitution:

ARTICLE I.

This organization shall be known as the National Association for the Study of Pellagra.

ARTICLE II.

The membership of this association shall be composed of medical and scientific workers, who are interested in the prevention, study and control of pellagra. The charter members of this association shall be selected by the Board of Directors hereinafter provided for, from the list of attending physicians registered at the National Conference on Pellagra held at Columbia, S. C., November 3 and 4, 1909.

ARTICLE III.

The officers of this association shall be a President, a First Vice President, a Secretary, Treasurer and Board of Directors.

ARTICLE IV.

The President, First Vice President, Secretary and Treasurer shall be elected annually and shall hold their offices for a period of one year, or until their successors are elected. The First Vice President, Secretary and Treasurer, together with four or more members, whose manner of selection shall be provided for in the By-Laws, shall constitute the Board of Directors.

ARTICLE V.

The meetings of this association shall be held annually at such time and place as may be agreed upon by a majority of the members present at the annual meeting preceding.

ARTICLE VI.

This association shall provide By-Laws, Rules and Regulations, not otherwise provided for, governing its deliberations, and the President shall have power to appoint committees to provide the By-Laws, Rules and Regulations above enumerated.

ARTICLE VII.

This Constitution may be amended at any annual meeting by a majority vote of all members present; provided that notice of such proposed amendment and vote thereon has first been publicly announced at a previous session of said meeting.

Officers 1909-1912

President,

DR. J. W. BABCOCK, Columbia, S. C.

First Vice President,

DR. W. A. WHITE, Washington, D. C.

Second Vice President,

DR. C. F. WILLIAMS, Columbia, S. C.

Secretary-Treasurer,

DR. G. A. ZELLER, Peoria, Ill.

Board of Directors,

DR. C. H. LAVINDER, U. S. P. H. Service, Washington, D. C.
DR. J. F. SILER, Med. Corps. U. S. Army, Washington, D. C.
DR. J. M. KING, Nashville, Tenn.
DR. J. J. WATSON, Columbia, S. C.

Local Committees:

General Committee of the South Carolina Medical Association: Drs. J. A. Hayne, Chairman, Columbia; Robert Wilson, Jr., Charleston; D. B. Frontis, Ridge Spring; G. A. Neuffer, Abbeville; Theodore Maddox, Union; J. J. Watson, Columbia; H. E. McConnell, Chester, and A. M. Brailsford, Mullins, and Hon. E. J. Watson, Columbia.

Executive Committee: Drs. J. W. Babcock, J. A. Hayne, and J. J. Watson.

Committee of Arrangements of the Columbia Medical Society: Drs. H. W. Rice, C. F. Williams, and J. LaB. Ward.

All meetings were held in the Assembly Hall of the State Hospital for the Insane, Elmwood Avenue and Bull Street.

Officers 1912-1915

President,

Dr. C. H. Lavinder, Surgeon, U. S. Public Health Service.

First Vice President,

Dr. J. F. Siler, Captain, Medical Corps, U. S. Navy.

Second Vice President,

Dr. C. C. Bass, Professor in Tulane University, New Orleans.

Secretary,

Dr. J. W. Babcock, Columbia, S. C.

Treasurer,

Dr. J. A. Hayne, State Health Officer, Columbia, S. C.

Board of Directors,

Dr. J. J. Watson, Columbia, S. C.

Dr. P. E. Garrison, U. S. Navy.

Dr. K. H. Beall, Fort Worth, Texas.

Dr. L. J. Pollock, Kankakee, Ill.

Programme

October 3, 10:30 A. M.

Invocation.

Address of Welcome.

Responses.

Address of President.

Appointment of Committees.

Registration of Members.

I. ETIOLOGY, EPIDEMIOLOGY AND STATISTICS.

"A Preliminary Report on the Epidemiology of Pellagra."
By the Thompson-McFadden Pellagra Commission.
Dr. J. F. Siler, Captain, Medical Corps, U. S. Army.
Dr. P. E. Garrison, Assistant Surgeon, U. S. Navy.
Dr. W. J. MacNeal, Assistant Director of Laboratories, Post Graduate Medical School, New York City.

"The Prevalence and Geographic Distribution of Pellagra in the United States."
Dr. C. H. Lavinder, Surgeon, U. S. Public Health Service.

"Epidemiology of Pellagra in the United States."
Dr. R. M. Grimm, Assistant Surgeon, U. S. Public Health Service.

"The Practical Handling of the Spoiled Corn Problem."
Hon. E. J. Watson, Commissioner of Agriculture, Columbia.

"One of the Possible Factors in the Causation of Pellagra."
Allan H. Jennings and W. V. King, Bureau of Entomology, Department of Agriculture, Washington.

"The Sand Fly and Pellagra."
Professor S. J. Hunter, State Entomologist, Lawrence, Kansas.

"Sambon, the Man, and His Later Investigations of Pellagra."
Dr. J. H. Taylor, Columbia.

"Some Further Observations in Regard to the Etiology of Pellagra."
Dr. M. L. Ravitch, Louisville.

Reports of Committees.

II. LOCAL HISTORY AND DIAGNOSIS OF PELLAGRA.

2:30 P. M.

"Pellagra in Rhode Island."
Dr. A. H. Harrington, Superintendent, State Hospital, Howard.

"History of Pellagra in the State of New York."
Dr. F. C. Curtis, Consulting Dermatologist, State Board of Health, Albany.

"Pellagra in Wisconsin."
Dr. O. H. Foerster, Milwaukee.

"Pellagra in Maryland."
Dr. C. W. G. Rohrer, Bureau of Communicable Diseases, Baltimore.

"Pellagra in the District of Columbia."
Dr. H. H. Hazen, Clinical Professor of Dermatology, Howard University, Washington.

"The Geographical Distribution of Pellagra in North Carolina and Its Significance."
Dr. E. J. Wood, Wilmington.

"Some Observations in Two Hundred and Seventy-six Cases of Pellagra Reported to the Tennessee State Board of Health."
Dr. J. C. Brooks, Chattanooga.

"Pellagra in Texas."
Dr. K. H. Beall, Member State Board of Health, Fort Worth.

"Pellagra in the Canal Zone."
Dr. W. E. Deeks, Isthmian Canal Commission.

"Pellagra in Bahamas."
Dr. J. A. Mackintosh, Abaco.

"Pellagra in Puerto Rico."
Dr. G. C. Watertton, Superintendent Insane Asylum, San Juan, Puerto Rico.

Reports of Committees.

OCTOBER 3D, 8:30 P. M.

III. SYMPOSIUM ON PELLAGRA.

"The Problem of Pellagra."
Surgeon General Rupert Blue, United States Public Health Service, Washington.

"Can Pellagra Be a Disease Due to Deficiency in Nutrition?"
Dr. F. M. Sandwith, Vice President Tropical Section International Medical Congress, 1913, London.

"Special Points of Epidemiological Interest in Pellagra."
Dr. Louis W. Sambon, London, England.

"Considerations as to the Etiology of Pellagra."
Drs. B. Gosio, Rome, and G. Antonini, Milan.

"Studies in Pellagra."
Prof. Victor Babes, Pathological Institute, Bucharest, Rumania.

"Contribution to the Study of the Alimentary Balance in Pellagrins."
Dr. Jean Nicolaidi, Paris, France, and Dr. Umberto Grillo, Martignacco, Italy.

"Anaphylactic Reaction in Pellagrins After Inoculation With Aqueous Extract of Spoiled Corn."
Drs. Volpino, Mariani, Bordoni, and Alpago-Novello, Institute of Hygiene, University of Turin, Italy.

"Bacteriological Investigations in Pellagra."
Dr. Eugenio Bravetta, Provincial Asylum, Milan.

"Pellagrous Insanity in Egypt."
Dr. R. W. J. Pearson, Subdirector of the Government Hospital for the Insane, Abbassia, Cairo, Egypt.

Reports of Committees.

OCTOBER 4TH, 10:30 A. M.

IV. LABORATORY INVESTIGATIONS OF PELLAGRA.

"Studies in the Metabolism of Moulds Belonging to the Genus Penicillium."
Drs. C. L. Alsberg and O. F. Black, Bureau of Plant Industry, Department of Agriculture, Washington.

"Preliminary Results of the Feeding of Penicillium Puberulum, Baimer."
Drs. H. Marsh and C. L. Alsberg, Bureau of Plant Industry, Department of Agriculture, Washington.

"Studies of the Nervous Histo-Pathology of Pellagra."
Drs. H. Douglas Singer and L. J. Pollock, State Psychopathic Institute, Hospital, Ill.

"Some Findings in the Cerebro-Spinal Fluid of Insane Pellagrins."
Dr. S. S. Hindman, Pathologist State Sanitarium, Milledgeville.

"The Experimental Production of Lesions Resembling Pellagra."
Dr. Herman M. Adler, Psychopathic Department, State Hospital, Boston.

"Intestinal Parasites of Pellagrins and Nonpellagrins."
Dr. Ernest Cooper, Pathologist, State Hospital, Columbia.

"The Specific Fluorescent Substances Present in the Blood Serum of Pellagrins."
Dr. A. D. Hirschfelder, Baltimore.

"The Chemistry of Spoiled Corn and Its Possible Relation to Pellagra."
Dr. H. S. Reed, Plant Pathologist, Agricultural Experiment Station, Blacksburg, Va.

V. CLINICAL FEATURES OF PELLAGRA.

"Early and Undeveloped Cases of Pellagra."
Dr. Beverly R. Tucker, Richmond.

"The Importance of Mild Cases of Pellagra in the General Consideration of the Subject."
Dr. C. C. Bass, Assistant Professor of Tropical Medicine and Clinical Medicine, Tulane University, New Orleans.

"Pellagra Erythema and Its Significance."
Dr. J. G. Wilkinson, Ragland, Ala.

"The Analogies of Pellagra."
Dr. Stewart R. Roberts, Associate Professor of the Practice of Medicine, College of Physicians and Surgeons, Atlanta.

"Etiologic Factors in Recurrent Attacks of Pellagra."
Dr. Geo. C. Mizell, Atlanta.

"Clinical and Pathological Notes on Pellagra."
Dr. C. W. G. Rohrer, Department of Health, Baltimore.

"A Case of Beri-Beri With Erythema Resembling Pellagra."
Dr. Robert Wilson, Jr., Chairman State Board of Health. Charleston.

"The Coexistence of Pellagra and Beri-Beri."
Dr. Eleanora B. Saunders, State Hospital, Columbia.

"Pellagra Among Children in Orphanages, With Observations on Eighty-five Cases in Two Institutions."
Dr. H. W. Rice, President Columbia Medical Society and Acting Physician to the Epworth Orphanage, Columbia.

"Clinical Picture in Insane Pellagrins Showing Interesting Findings in Spinal Fluid."
Dr. J. W. Mobley, First Assistant Physician, State Sanitarium, Milledgeville.

"The Eye Symptoms of Pellagra"—A Second Report.
Dr. E. M. Whaley, Oculist, State Hospital, Columbia.

Reports of Committees.

OCTOBER 4TH, 2:30 P. M.

VI. TREATMENT OF PELLAGRA.

"The Treatment of Pellagra: Its Present Status."
Dr. G. M. Niles, Professor of Gastro-Enterology and Therapeutics, Atlanta School of Medicine, Atlanta.

"The Treatment of Pellagra."
Dr. J. J. Watson, Columbia.

"Pellagra: Its Treatment."
Dr. E. H. Bowling, Durham.

"Care of the Alimentary Tract in Pellagrins."
Dr. A. Moultrie Brailsford, Jr., Mullins, S. C.

"Results of Transfusion in Thirty-five Cases of Pellagra."
Dr. H. P. Cole, Mobile.

"The Relative Value of Soamin and Salvarsan in the Specific Treatment of Pellagra."
Dr. E. H. Martin, Hot Springs, Ark.

"Salvarsan in Pellagra: Final Report."
Dr. W. J. Cranston, Assistant Physician, State Sanitarium, Milledgeville.

"The New Serum Treatment of Pellagra."
Dr. W. C. Brownson, Asheville.

"The After Effects of Nicolaidi's Organo-Polymieralized Serum in the Treatment of Pellagra."
Dr. J. Vernesco, Director of the Preda Hospital, Craiova, Rumania.

"Later Results on Pellagrins Subjected to Nicolaidi's Serum Therapy in 1911."
Dr. Umberto Grillo, Martignacco, and Dr. Emilio Maj, Vice Director of the Insane Hospital, Udine, Italy.

"Two Cases of Pellagra in Rumania With Grave Nervous Phenomena, Cured in a Short Time With Nicolaidi's Serum."
Dr. Jean Nicolaidi, Paris, France.

VII. MISCELLANEOUS ASPECTS OF PELLAGRA.

"Is Pellagra Communicable?"
Dr. J. A. Hayne, Secretary and Health Officer, State Board of Health, Columbia.

"Medico-Legal Relations of Pellagra."
Dr. J. W. Babcock, State Hospital, Columbia.

"Dental Findings in Insane Pellagrins."
Dr. S. F. Killingsworth, Dentist, State Hospital, Columbia.

"The Sociological Side of Pellagra."
L. B. Myers, General Secretary, Associated Charities, Charlotte.

Reports of Committees.

8:30 P. M.

Additional Papers.

Reports of Committees.

Lantern Slide Exhibition of Pellagra.

Members Registered

1912

Dr. Rupert Blue.....Washington, D. C.
Dr. Beverley R. Tucker.....Richmond, Va.
Dr. W. W. Wothers.....Orlando, Fla.
Dr. W. B. Way.....Ridgeville, S. C.
Dr. C. C. Bass.....New Orleans, La.
Dr. J. Q. Coleman.....Shelton, S. C.
Dr. J. R. Campbell.....Clover, S. C.
Dr. J. L. Thompson.....Columbia, S. C.
Dr. Robert Black.....Bamberg, S. C.
Dr. S. S. Hindman.....Milledgeville, Ga.
Dr. S. S. Sarratt.....Union, S. C.
Dr. D. L. Bryson.....Grey Court, S. C.
Dr. E. H. Martin.....Hot Springs, Ark.
Dr. L. A. Riser.....Columbia, S. C.
Dr. S. T. Brasington.....Camden, S. C.
Dr. Geo. M. Niles.....Atlanta, Ga.
Dr. H. H. Griffin.....Columbia, S. C.
Dr. John B. Ray.....Leaksville, N. C.
Dr. F. A. Coward.....Columbia, S. C.
Dr. R. A. Lancaster.....Columbia, S. C.
Dr. P. E. Garrison.....U. S. Navy
Dr. W. E. Sparkman.....Georgetown, S. C.
Dr. C. N. Wyatt.....Easley, S. C.
Dr. John B. Wright.....Lincolnton, N. C.
Dr. W. A. Monroe.....Sanford, N. C.
Dr. Jas. A. Turner.....High Point, N. C.
Mr. W. V. King.....Washington, D. C.
Dr. F. D. Rodgers.....Columbia, S. C.
Dr. D. S. Pope.....Columbia, S. C.
Dr. W. H. Dial.....Laurens, S. C.
Dr. W. J. Cranston.....Milledgeville, Ga.
Dr. S. M. Pitts.....Saluda, S. C.
Dr. J. C. Lawson.....Darlington, S. C.

Dr. Sophia Brunson.....St. Matthews, S. C.
Dr. A. S. Townsend.....Bennettsville, S. C.
Dr. Sam Wall.....Centenary, S. C.
Dr. Robert Wilson, Jr.....Charleston, S. C.
Dr. W. M. Lester.....Columbia, S. C.
Prof. S. J. Hunter.....Lawrence, Kan.
Dr. R. E. Mathias.....Irmo, S. C.
Dr. J. S. Hopkins.....Hopkins, S. C.
Dr. E. A. Hines.....Seneca, S. C.
Dr. W. J. Burdell.....Camden, S. C.
Dr. D. B. Frontis.....Ridge Spring, S. C.
Dr. T. L. W. Bailey.....Clinton, S. C.
Dr. W. G. Houseal.....Newberry, S. C.
Dr. C. F. Williams.....Columbia, S. C.
Dr. A. J. Christopher.....Laurens, S. C.
Dr. W. D. Ferguson.....Laurens, S. C.
Dr. W. A. Sheldon.....Liberty, S. C.
Dr. A. H. Harrington.....Howard, R. I.
Dr. H. Douglas Singer.....Hospital, Ill.
Dr. J. F. Siler.....U. S. Army
Dr. O. S. Hillman.....New York City, N. Y.
Dr. V. C. Myers.....New York City, N. Y.
Dr. W. J. MacNeal.....New York City, N. Y.
Mr. Allan H. Jennings.....Washington, D. C.
Dr. Miles B. Cope.....Port Royal, S. C.
Dr. W. C. Abel.....Columbia, S. C.
Dr. W. A. Tripp.....Easley, S. C.
Dr. V. W. Brabham.....Cope, S. C.
Dr. Thos. N. Dulin.....Clover, S. C.
Dr. S. B. Fishburne.....Columbia, S. C.
Dr. James A. Hayne.....Columbia, S. C.
Dr. W. Egleston.....Hartsville, S. C.
Dr. F. A. Boaz.....Stoneville, N. C.
Dr. C. W. G. Rohrer.....Baltimore, Md.
Dr. A. H. Vandivert.....St. Joseph, Mo.
Dr. S. T. D. Lancaster.....Spartanburg, S. C.
Dr. L. J. Pollock.....Kankakee, Ill.
Dr. A. Clifton Smith.....Glenn Springs, S. C.
Dr. T. W. Carmichael.....Rowland, N. C.

Dr. C. A. Teague.....Graniteville, S. C.
Dr. K. N. Beall.....Fort Worth, Texas
Dr. T. J. Picot.....Raleigh, N. C.
Dr. Gordon Chason.....Bainbridge, Ga.
Dr. W. L. Athon.....Anna, Ill.
Dr. R. N. Greene.....Chattahoochee, Fla.
Dr. H. H. Hazen.....Washington, D. C.
Dr. Carl L. Alsberg.....Washington, D. C.
Dr. R. M. Grimm.....U. S. Public Health Service
Dr. H. W. Adler.....Boston, Mass.
Dr. C. H. Lavinder.....U. S. Public Health Service
Dr. A. D. Hirschfelder.....Baltimore, Md.
Dr. W. S. Partlow.....Tuscaloosa, Ala.
Dr. Geo. H. Searcy.....Tuscaloosa, Ala.
Dr. W. C. Brownson.....Asheville, N. C.
Dr. J. J. Watson.....Columbia, S. C.
Dr. H. E. McConnell.....Chester, S. C.
Dr. Verner Nesbit.....Kansas City, Mo.
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Dr. J. D. Willis.....Roanoke, Va.
Dr. W. R. Wallace.....Chester, S. C.
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Dr. Stewart R. Roberts.....Atlanta, Ga.
Dr. W. E. Deeks.....Panama
Dr. E. H. Bowling.....Durham, N. C.
Dr. Jas. E. Poore.....Columbia, S. C.
Dr. John Lyon.....Ninety-Six, S. C.
Dr. E. R. Goodyear.....Greenwood, S. C.
Dr. Ernest Cooper.....Columbia, S. C.
Dr. W. L. Kirkpatrick.....Pacolet, S. C.
Dr. C. W. Barron.....Columbia, S. C.
Dr. C. L. Kibler.....Columbia, S. C.
Dr. F. M. Durham.....Columbia, S. C.
Dr. C. E. Young.....Columbia, S. C.
Dr. Baxter Hayne.....Spartanburg, S. C.
Dr. Henry Norris.....Rutherfordton, N. C.
Dr. J. W. Payne.....Epworth, S. C.
Dr. J. M. Barfield.....Linesville, Ala.
Dr. J. O. Elrod.....Forsythe, Ga.

Dr. T. P. Kennedy.....Union, S. C.
Dr. H. W. Rice.....Columbia, S. C.
Dr. F. W. P. Butler.....Columbia, S. C.
Dr. Geo. C. Mizell.....Atlanta, Ga.
Dr. C. W. Gould.....Atlanta, Ga.
Dr. W. D. Ouzts.....Edgefield, S. C.
Dr. J. W. Bell.....Walhalla, S. C.
Dr. W. W. Ray.....Congaree, S. C.
Dr. T. M. DuBose.....Columbia, S. C.
Dr. Geo. F. Powell.....Terrell, Texas
Dr. R. B. Epting.....Greenwood, S. C.
Dr. G. A. Neuffer.....Abbeville, S. C.
Dr. G. F. Neel.....Greenwood, S. C.
Dr. W. T. Lander.....Williamston, S. C.
Dr. S. G. Miller.....Chester, S. C.
Dr. M. W. Chambers.....Jonesville, S. C.
Dr. Eleanora B. Saunders.....Columbia, S. C.
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Dr. C. A. Foster.....Timmonsville, S. C.
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Dr. Charles R. Taber.....Dillon, S. C.
Dr. W. O. Nesbit.....Charlotte, N. C.
Dr. J. La Bruce Ward.....Columbia, S. C.
Dr. J. W. Babcock.....Columbia, S. C.
Dr. D. S. Currie.....Parkton, N. C.
Dr. D. A. Garrison.....Gastonia, N. C.
Dr. H. T. Glenn.....Gastonia, N. C.
Dr. L. Rosa H. Gantt.....Spartanburg, S. C.
Dr. S. G. Laws.....Spartanburg, S. C.
Mr. L. B. Myers.....Charlotte, N. C.
Dr. J. H. Roberts.....Ehrhardt, S. C.
Dr. J. Lee Young.....Clinton, S. C.
Dr. A. B. Knowlton.....Columbia, S. C.
Dr. Theodore Maddox.....Union, S. C.
Dr. O. S. C. Jackson.....Union, S. C.
Dr. N. B. Edgerton.....Columbia, S. C.
Dr. W. G. White.....Yorkville, S. C.
Dr. I. Schayer.....Laurens, S. C.
Dr. W. R. Barron.....Columbia, S. C.

Charter Members

November, 1909

B. L. Eiker.....Leon, Iowa
Jno. H. Miller.....Cross Hill, S. C.
E. W. Pinson.....Cross Hill, S. C.
S. T. Cade.....Wilmington, N. C.
J. D. Jones.....Sweetwater, Ala.
J. M. Buchanan.....Meridian, Miss.
D. J. Williams.....Ellisville, Miss.
W. J. Burdell.....Lugoff, S. C.
E. M. Mason.....Montgomery, Ala.
Walter H. Bublie.....Chicago
Gardner T. Swarts.....Providence, R. I.
W. C. Woodward.....Washington, D. C.
Herbert Fox.....Philadelphia
Carl L. Alsberg.....Washington, D. C.
Manfred Hall.....Richmond, Va.
E. W. P. Gavock.....Richmond, Va.
B. R. Tucker.....Richmond, Va.
Jno. W. Thomas.....Pineville, La.
W. M. Love.....McConnellsville, S. C.
J. F. Siler.....Med. Corps, U. S. Army
H. J. Nichols.....Med. Corps, U. S. Army
H. Douglas Singer.....Kankakee, Ill.
O. C. White.....Chicago
L. J. Pollock.....Chicago
W. J. MacNeal.....Urbana, Ill.
H. S. Grindley.....Urbana, Ill.
William Whitford.....Journal A. M. A., Chicago
John Forrest.....Charleston, S. C.
John Lunny.....Darlington, S. C.
C. B. McKeown.....Fort Lawn, S. C.
W. B. Cox.....Chester, S. C.
J. P. Yongue.....Richburg, S. C.
S. F. Brasington.....Camden, S. C.

E. C. Brasington.....Kershaw, S. C.
Meade Ferguson.....Richmond, Va.
H. T. Chapin.....Pittsboro, N. C.
N. J. Strickland.....Moncure, N. C.
Louis M. Warfield.....Savannah, Ga.
V. H. Bassett.....Savannah, Ga.
S. P. Watson.....Loris, S. C.
J. K. Gilder.....Newberry, S. C.
J. M. Johnson, Ph. D.....Newberry, S. C.
C. C. Gambrell.....Abbeville, S. C.
A. E. B. Heford.....Greensboro, N. C.
W. DeK. Wylie.....Richburg, S. C.
Jas. C. Moore.....McColl, S. C.
D. A. Garrison.....Gastonia, N. C.
Thos. N. Dulin.....Clover, S. C.
R. C. Brown.....Lancaster, S. C.
J. R. Miller.....Rock Hill, S. C.
Dowd K. Briggs.....Blakesville, S. C.
T. W. Carmichael.....Bennettsville, S. C.
T. B. Salters.....Blenheim, S. C.
Chas. R. May.....Bennettsville, S. C.
J. H. Downey.....Gamewell, Ga.
Jas. A. Burroughs.....Asheville, N. C.
Hastings Wyman.....Aiken, S. C.
Louis Leroy.....Memphis, Tenn.
J. A. Albright.....Nashville, Tenn.
B. G. Tucker.....Nashville, Tenn.
W. E. Hibbet.....Nashville, Tenn.
Robert Black.....Bamberg, S. C.
T. E. Wannamaker, Jr.....Cheraw, S. C.
Thos. D. Coleman.....Augusta, Ga.
Charles L. Minor.....Asheville, N. C.
L. E. Buel.....Cheraw, S. C.
W. L. Dunn.....Asheville, N. C.
Jno. W. Parker.....Williamston, S. C.
J. R. Young.....Anderson, S. C.
Raymond Elgin.....Searles, Ala.
Jas. R. Anderson.....Morganton, N. C.
J. D. Long.....U. S. P. H. and M. H. Service

C. H. Lavinder.....U. S. P. H. and M. H Service
Edward Frances.....U. S. P. H. and M. H. Service
I. W. Faison.....Charlotte, N. C.
M. J. Walker.....Yorkville, S. C.
J. W. Campbell.....Clover, S. C.
B. C. Moore.....Pageland, S. C.
B. M. Badger.....Dillon, S. C.
Sam Mace.....Centenary, S. C.
J. F. Shirley.....Honea Path, S. C.
Jno. R. Erwin.....Charlotte, N. C.
Walter Cheyne.....Sumter, S. C.
T. B. Ray.....Leaksville, S. C.
J. E. S. Davidson.....Charlotte, N. C.
D. G. Caldwell.....Concord, N. C.
T. Grange Simons.....Charleston, S. C.
H. F. Harris.....Atlanta, Ga.
J. M. Kibler.....Newberry, S. C.
C. L. Kibler.....Columbia, S. C.
A. A. Madden.....Columbia, S. C.
W. A. Tripp.....Easley, S. C.
John Lyon.....Ninety-Six, S. C.
G. P. Neel.....Greenwood, S. C.
J. E. Brunson.....Ninety-Six, S. C.
C. N. Wyatt.....Easley, S. C.
J. Swinton Whaley.....Edisto Island, S. C.
A. M. Redfearn.....Clemson College, S. C.
W. C. Abel.....Columbia, S. C.
S. B. Sherard.....Gaffney, S. C.
D. M. Crosson.....Leesville, S. C.
P. M. Connor.....Leesville, S. C.
O. L. P. Jackson.....Union, S. C.
S. G. Sarratt.....Union, S. C.
A. W. Browning.....Elloree, S. C.
O. F. Portwood.....Timmonsville, S. C.
R. K. Foster.....Timmonsville, S. C.
T. M. Hitch.....Hodges, S. C.
J. D. McDowell.....Yorkville, S. C.
L. C. Brooker.....Swansea, S. C.
W. M. Brockinton.....Manning, S. C.

F. C. Hinson.....Lancaster, S. C.
W. G. White.....Yorkville, S. C.
Crown Torrence.....Union, S. C.
H. T. Bahnson.....Winston-Salem, N. C.
C. B. Earle.....Greenville, S. C.
R. B. Jarrett.....Central, S. C.
Wm. A. Woodruff.....Catechee, S. C.
S. C. Baker.....Sumter, S. C.
C. A. Speisegger, Jr.....Charleston, S. C.
D. B. Frontis.....Ridge Spring, S. C.
McM. K. Mazyck.....Charleston, S. C.
Francis B. Johnson.....Charleston, S. C.
W. D. Ferguson.....Laurens, S. C.
F. A. Smith.....Mullins, S. C.
S. T. D. Lancaster.....Spartanburg, S. C.
N. H. Jennings.....Bishopville, S. C.
R. D. McCutcheon.....Bishopville, S. C.
J. C. Lawson.....Darlington, S. C.
R. B. Epting.....Greenwood, S. C.
F. R. Geiger.....New Brookland, S. C.
Jesse H. Teague.....Laurens, S. C.
C. A. McLurkin.....Chester, S. C.
W. O. Holloway.....Chappels, S. C.
Jno. L. Dawson.....Charleston, S. C.
Davis Furman.....Greenville, S. C.
J. S. Rhame.....Camden, S. C.
J. Howell Way.....Waynesville, N. C.
James Ely.....Logan, N. C.
L. G. Hardman.....Commerce, Ga.
Thos. W. Murrell.....Richmond, Va.
Howard Fox.....New York City
Jno. F. Coleman.....Olar, S. C.
T. T. Merriweather.....Asheville, N. C.
Isaac M. Taylor.....Morganton, N. C.
J. H. Roberts.....Eberhardt, S. C.
J. H. Fender.....Eberhardt, S. C.
Jno. B. Wright.....Lincolnton, N. C.
M. S. Rock.....Greenville, S. C.
J. I. Bedenbaugh.....Prosperity, S. C.

E. W. Warren.....Palatka, Fla.
L. Boyd.....Rock Hill, S. C.
John M. McConnell, Ph. D.....Davidson College, N. C.
J. F. Watson.....Lamar, S. C.
J. W. Babcock.....Columbia, S. C.
F. H. McLeod.....Florence, S. C.
D. S. Pope.....Columbia, S. C.
E. M. Whaley.....Columbia, S. C.
W. H. Dial.....Laurens, S. C.
W. R. Dendy.....Pelzer, S. C.
W. B. Hough.....Jefferson, S. C.
J. R. McCormack.....Olar, S. C.
J. J. Watson.....Columbia, S. C.
W. S. Boyd.....Salters, S. C.
C. F. Williams.....Columbia, S. C.
J. W. Bell.....Walhalla, S. C.
W. E. Pelham.....Newberry, S. C.
Z. E. Pinner.....Pomaria, S. C.
O. D. Hammond.....Blackville, S. C.
J. Bennett Townsend.....Anderson, S. C.
W. D. Simpson.....Abbeville, S. C.
C. M. Walker.....Westminster, S. C.
J. H. Taylor.....Columbia, S. C.
J. E. Edwards.....Spartanburg, S. C.
N. A. White.....Washington, D. C.
B. G. Tucker.....Nashville, Tenn.
H. E. McConnell.....Chester, S. C.
B. G. Gregg.....Florence, S. C.
J. L. McGilman.....Holly Hill, S. C.
W. M. Carn.....Columbia, S. C.
Ward H. Mills.....The State, Columbia, S. C.
J. T. Meehan.....The Associated Press, Columbia, S. C.
Garnault Agassiz.....National Magazine
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I. Introductory

THE PROBLEM OF PELLAGRA IN THE UNITED STATES.

By Rupert Blue, D. Sc., M. D., Surgeon General U. S. Public Health Service, Washington, D. C.

Mr. Chairman, Ladies and Gentlemen:

In the evolutionary scheme of the universe the weaker members of the primal race succumbed, while the remainder, having the courage and tenacity to meet and conquer their enemies, developed into men.

And so this meeting tonight is the outward and visible manifestation of this evolutionary process toward the Golden Age, which, though we may never bring it to pass in its full fruition, we may dream about and labor towards, and in this is the blessedness of our quest for the unattainable ideal—"for to travel hopefully is a better thing than to arrive, and the true success is labor." The fight is worthy of our swords, and already the eagles of victory hover over the standard-bearers who are leading in the combat with pellagra. Already the scouts of science have reconnoitered the enemy's position, and I predict that it will not be long until the signal for the general assault will be sounded and the works of our foeman stormed and taken. The success which will crown the banner of Hygeia in this fray will bring relief and protection to countless thousands, and the future will see the subjugation of this enemy which mars the exterior of the human form and unhinges the portals of the mind.

Man born of woman has been assailed from time immemorial by plagues, pestilence and famine. Applied husbandry and improved methods of cultivation have averted the danger of the latter, and the unselfish labors of medical scientists have lain the ghosts of disease which once roamed the land in the darkness of ignorance and human misery. So encouraging have been the results of this battle for the freedom of man from the thralldom of disease that we have reason to hope that the banishment of the enemy against whom we are now met in council of war is not far distant.

Pellagra presents one of the most difficult problems with which we have to deal. It is difficult because we know practically nothing

of its cause, nor mode of transmission from man to man, or whether it is transmitted by man at all. If the cause and nature of the disease were known, steps could be taken toward its cure and eradication; but, as a matter of fact, our knowledge of the disease today is almost as faulty as it was fifty years ago.

There are at the present time four well defined theories as to the causal agents, namely: infection, intoxication, auto-intoxication, and food "deficiency." I shall consider only the first and fourth of the series, as they promise important developments in the future. This selection, I should state, is entirely arbitrary, and represents the opinion of the writer alone.

Some of the exponents of infection are Ceni, di Pietro and Tizzone, each of whom has found different micro-organisms either in maize or in the bodies of patients and which they credit with the power of producing the disease. Their claims are based upon an enormous amount of experimental work. They still lack confirmation.

Sambon, of London, advanced the protozoal theory, and strengthened his hypothesis by an extensive field investigation of the pellagrous districts of Roumania and Italy. He believes that the disease is transmitted from man to man by the bite of a fly, the *Simulium reptans*. These conclusions, however, are based entirely upon field studies, and as yet there are no laboratory findings to confirm them. The hypothesis of Sambon forms the basis of extensive studies in America, which should be amplified and continued. This investigator denies that maize eating has any bearing on the causation of the disease.

Prof. Allesandrini, of Italy, is credited with the nematode hypothesis, the infection, according to that investigator, being derived from a worm which is found in running water. Drs. Lavinder and Babcock state that the etiology is still an open question, and it must be admitted that this conclusion is entirely correct. Too much cannot be said in praise of the splendid work of the men now engaged in the attempt to solve this problem, and we Americans, particularly we South Carolinians, should be proud of the showing which the gentlemen just referred to have made.

A second promising line of investigation as regards the causation of the disease is to be found in the deficiency theory as advanced by Casimir Funk. He states that "it is beyond any doubt that

pellagra has some close connection with maize diet." Pellagra is thus placed in the same category with scurvy and beri-beri. It is only in the case of an exclusive or one-sided diet of corn; and, if the corn is spoiled, it is all the more deficient in nutritive values.

It will be seen that the corn doctrine of the "Zeist" school is not entirely rejected nor is it confirmed by the researches of Dr. Funk. It means that if corn, either spoiled or sound, is used as an exclusive diet, certain symptoms will appear. Similarly, if a rice diet is persisted in, the syndrome known as beri-beri will follow.

So far the discussion has only increased our perplexity and served to emphasize the necessity of renewed activity in both laboratory and field in the hope of finding the causal agents of the disease. Indeed, the great need of study and investigation to uncover the modes of dissemination is one of the pressing questions of the hour. Under such conditions, the sanitarian is at a loss to know how to approach the problem of prevention, and is forced to fall back on the general principles of his science. It is true, a line of action may be opened up from the standpoint of hygiene, since most observers agree that bad hygienic conditions, poor food and poverty are predisposing factors.

It follows that the remedy for our lack of knowledge lies in scientific investigation. It is hoped that research work will expose the bare facts, and in time give us the working hypothesis desired. To accomplish this money is needed and authority required.

Appropriations for such a purpose are in the long run a measure of great economy, because of the serious economic losses now produced every day by this disease. The amount spent by the various States in the care of pellagrins is so great that it warrants large expenditures for the solution of the problem of preventing the disease.

Thus far the burden has been borne by the States, but it should be recognized that this is a national danger—one which seriously afflicts the citizens of many States, and acts as a deterrent of progress and prosperity in many communities. Therefore the Federal health agency should be supplied with funds to be used in co-operation with those States requesting government aid in the matter.

The general public should take a keen interest in this problem, and urge our lawmakers, State and Federal, to allow appropriations

to be made for this work. Traditions in regard to the diseases with which you are familiar should not be allowed to survive or to retard your active interest in this matter.

It is rather a sad commentary on our business astuteness that we have failed to recognize the economic importance of protecting the public health. While we are depending on lax laws and underpaid officials to bring about better conditions, the main factor of the problem is overlooked entirely.

It is a mistaken policy to conceal the facts of sanitary interest from the general public. It is due to the citizens of the United States that they be kept fully informed as to the progress of diseases and the localities in which infection is known to exist. We can by such means awaken an interest in the public health and stimulate many to inquire into the cause and cure of disease.

The care, preservation and preparation of foods have of late years assumed an importance not heretofore known or suspected. Badly prepared and poorly preserved foods are unwholesome, and inasmuch as pellagra is found so often among the poor, it may be due, at least in part, to bad cooking, and to the general insanitary conditions which are the inevitable accompaniments of poverty.

All of this is a matter of the greatest importance to the American nation. Since Harris, of Georgia, and Searcy, of Alabama, first announced the presence of the disease in the South, it has spread over no less than eight States and has been reported as existing in small foci in many more. Dr. Babcock, of Columbia, recognized the disease in South Carolina and brought it to the attention of the medical profession, thereby performing a praiseworthy labor which has proven of great value not only to the people of his own State and our nation, but to all the world. The widespread character of pellagra is well illustrated by data which has been collected by Dr. Lavinder, of the United States Public Health Service. Complete data are lacking, but the following statement will serve to give a fairly accurate idea.

The figures for the following eight States are based on replies received from cards sent to each individual physician in the entire eight States, and show the totals for the years 1907 to 1911 inclusive:

	Cases.	Deaths.
Kentucky	509	218
Virginia	622	344
North Carolina	2,502	1,067
South Carolina	1,880	582
Alabama	2,314	859
Georgia	4,558	1,582
Mississippi	2,877	1,240
Louisiana	660	291
	15,922	6,183

Replies to the cards sent out were received from less than 50 per cent. of the doctors; and from subsequent investigation it was evident that a great many cases remained unreported. It is very conservative to estimate at least 25 per cent. more cases than the above, or in round numbers not less than 20,000 cases in these eight States from 1907 to 1911.

The rapid increase of the disease may be judged from the following figures from these eight States:

	Cases.
1907	621
1908	1,036
1909	2,336
1910	4,598
1911	7,331
	15,922

Figures have not been compiled as yet for the other States, but the following estimates are based on known data and are believed to be very conservative:

	Total cases 1907-1911.
Maryland	350
Tennessee	3,500
Florida	50
Arkansas	500
Texas	2,500
Illinois and Pennsylvania	600
All other States	200
	7,700

These collected figures give us a total of 27,700 cases in the entire United States, including the calendar year 1911. The estimates are very conservative. The disease is still spreading and increasing everywhere, and certainly it is no exaggeration to say that up to the present date (September 1, 1912) there have been a total of not less than 30,000 cases of pellagra in the United States since 1907, when the disease first came into notice.

The case mortality of pellagra in the United States, computed on the exact figures for the eight States mentioned above—6,183 deaths in a total of 15,922 cases—is 38.83 per cent. The paucity of these statistics illustrates perfectly the need for a widespread investigation of the prevalence of this disease. Pellagra should be placed upon the list of reportable diseases in all of the States, and we should endeavor to map out accurately all of the foci in which it is found. This is the duty of the State and municipal health authorities, but the Federal government should not be lacking in lending its aid and co-operation in collecting accurate data regarding this disease which is, so to speak, a national scourge.

In the absence of knowledge as to the causal agent of the disease, it is impossible to lay down accurate prophylactic measures. For the present we must rely upon mixed diet of high nutrient value, and we must, of course, endeavor to secure good hygienic conditions wherever possible. In addition, the various States should establish places for the treatment of the unfortunate sufferers from the disease. The United States Public Health Service, by utilizing the Marine Hospital at Savannah, Ga., for this purpose, has set a good example.

In a movement of this kind we must have thorough co-operation and perfect teamwork. This implies that there are certain duties devolving upon the States, and certain duties devolving upon the Federal government. These duties should be performed in unison, the efforts of each interlocking with and aiding the other. To this end the measures above referred to should be carried out, and in addition the various States should report pellagra to the Federal health authority exactly as they are reporting the known communicable diseases at present. It is the duty of the Federal government, on the other hand, to study and investigate the disease in order that the tangled web of causation and dissemination may be unravelled

and the States given the basic facts which are necessary in the prophylaxis and eradication of this disease.

The Federal government should disseminate the information which it acquires in this way, and this should take on two forms: one, the placing in the hands of scientific workers the accurate knowledge obtained by field and laboratory studies; the other should be in the form of popular bulletins which can be read and taken to heart by all of the lay public.

It is to be hoped that the future will see an extension of the field and hospital studies. It is necessary that we determine why pellagra is a rural disease, as well as the reason for the terminal phase of insanity or paralysis. We are also perplexed as to the reason for its greater prevalence among females, and the fact that it seems to be a place-disease. The relation, if any, which the actinic rays of light bear to the eruption must also be studied, and it is necessary that the question of insect transmission be thoroughly worked out.

PRESIDENTIAL ADDRESS—HOW LONG HAS PELLAGRA EXISTED IN THE UNITED STATES?

By J. W. BABCOCK, M. D.

Ladies and Gentlemen:

It is nearly three years since this National Association for the Study of Pellagra was organized and held in this hall its first meeting. It has, therefore, seemed to some of its members that the time has arrived for another conference to consider the progress made, especially regarding the cause, prevention, and cure of the malady. Besides these there are many other phases of the subject, both old and new, that are well worthy of further attention and discussion. The meeting has again been called in Columbia in response to an invitation extended last April by the South Carolina Medical Association. These are the chief reasons which serve to explain our presence here today.

For the introductory address I have selected the topic: How Long Has Pellagra Existed in the United States? I choose this theme not only on account of its importance, but because I feel convinced that there are valuable lessons still to be learned from the historical side of this subject.

The rapid recognition of the widespread prevalence of pellagra in this country within the last five years constitutes a remarkable chapter in the history of medicine. Naturally, it has raised the questions: Has a new disease suddenly developed in epidemic form, or are we facing an extensive recrudescence of a condition formerly overlooked? It is to answer these questions that this study has been undertaken. It should be understood from the beginning, however, that the spirit of the inquiry is that of explanation and not of reprehension and adverse criticism. The effort will also be made to bring out the salient facts in the early and recent history of pellagra in our country.

What, then, is the explanation of this extraordinary episode in American medical history? When in 1908 the prevalence of pellagra in the United States first began to be generally recognized it seemed as if a new plague had stricken the people. To many physicians its recognition was a surprise if not a shock; while among

the laity in some places pellagraphobia has created a panic. Even today, for various reasons, in some hospitals and localities where its existence has been demonstrated, the presence of pellagra is either denied or unwillingly admitted. Further elucidation of the historical part of the problem is desired and expected, for doubtless there exist unknown or inaccessible to me, many records which, when discovered, will throw further light upon the subject. In the cause of truth, therefore, it is hoped that explanations and confessions, too, will yet be made by honest investigators and historians.

If pellagra has long been present in the United States, why has it not been recognized? Briefly, one reason is that American physicians had been taught that pellagra did not exist in their land. Its oversight has been due to the "thraldom of authority." To illustrate: In 1906 Osler[1] said: "Pellagra occurs extensively in parts of Italy, in the South of France, and in Spain. It has not been observed in the United States." As recently as August, 1907, Sir Patrick Manson[2] wrote: "There are vast regions in which maize is extensively cultivated and much eaten, but in which pellagra is absolutely unknown. A most convincing example is that of the United States of America." In Kurella's biography of Lombroso[3] the statement is made that Lombroso at one time "went so far as to believe that nothing could be done to save the peasants and small farmers from pellagra, as long as they remained in their north Italian homes, and he recommended a wholesale emigration to North America." Shortly before his death, Lombroso stated, however, to Dr. J. J. Watson that he had long suspected the existence of pellagra in the United States. It is now recalled that less than a decade ago one of the highest authorities on diagnosis in the United States, while visiting in South Carolina, failed to recognize a typical case of pellagra which had been referred to him by puzzled general practitioners. His final diagnosis was "Glossitis." Dr. F. M. Sandwith, the English pellagralogist, wrote[4] in 1909: "In spite of denial from American authorities on medicine, I have always suspected that pellagra might exist, unrecognized, in the South, and at one time I requested my friends to put me into communication with the poorest folk of the maize-eating districts. I was referred to a settlement in eastern Virginia for pauper negroes, but on investigation, I found that the inmates lived in stone houses on pork rations and I came to the conclusion that the word poverty represented no

condition in America which could compare with the misery of the impoverished peasants of Italy, Roumania, or Egypt." Dr. Sandwith further says[5] that in April, 1905, he had the good fortune to find a case of unrecognized pellagra in an Italian immigrant in the wards of the Boston (Mass.) City Hospital, where it had been classified with cases of epidemic cerebro-spinal meningitis. These citations from such authorities, in so far as the presence of pellagra in the United States is concerned, the problems are perhaps sufficient to indicate the former attitude of medical writers towards this disease.

To some teachers of medicine in this country pellagra was merely of academic interest, while to the majority of physicians even the name of the disease was scarcely known, or existed only as a vague memory.

Curiously enough, pellagra had been reported from South America (Brazil and the Argentine Republic), and from Mexico (Yucatan and Campeche). But as recently as last August the American Consul General at Buenos Ayres wrote me that exhaustive inquiries had failed to establish the existence of pellagra in the Argentine Republic. Lombroso had noted[6] the observation by Bahuino in 1600, of a disease, analogous to pellagra, among the American Indians following the use of maize. The early history of maize is obscure. Columbus is said to have found it in the West India Islands at the end of the fifteenth century. When Cartier visited Hochelaga, now called Montreal, in 1535, that town was situated in the midst of extensive cornfields. Capt. John Smith, in 1610, considered corn, in spite of its disadvantages, the best food for colonists. In 1620 the Pilgrims found quite extensive plantings of maize near Plymouth, Massachusetts.[7] Indian corn was also called "Guinny wheat," or "Turkie wheat" (Cf. Grano Turco. Ital.) by the colonists.[8] Furthermore, the incrimination of maize as a cause of disease is a part of the early but forgotten history of the colonization of the northern part of the United States. To cite one illustration: In Winthrop's Journal it is recorded:[9] "1641. November 12. The summer past was very cool and wet, so as much Indian corn never ripened, though some stood till the 20th of this month. It was observed that people who fed upon that corn were extraordinarily infected with worms in their bodies all the year following, which in some was well prevented by leaving

their bread, and feeding upon salt fish." Clearly, then, the relationship of Indian corn to the medical history of the early American colonist deserves further research and investigation.

In 1839 Dr. Pliny Earle, afterwards a distinguished asylum physician in this country, studied cases of pellagra at the Ospedale Maggiore in Milan. In spite of his subsequent extended experience in asylums of the United States, he seems not to have recorded any further observations of the disease, although he took part in the discussion of Dr. Gray's case in Washington in 1864, and was for many years superintendent of the Northampton, Massachusetts, asylum where pellagra has been observed this year (1912).

In spite of the persistent denial in recent years by high authorities, however, cases of pellagra, seemingly sporadic, had been reported in the United States. In 1864 reports of asylum cases were made by Drs. Gray and Tyler from New York and Massachusetts, respectively.[10] The authenticity of these cases has usually been admitted by recent American writers, though others have questioned or ignored them. These are probably the earliest printed reports of correctly diagnosticated cases of pellagra in this country, and it should be remembered that Gray and Tyler were well-informed and reliable alienists.

It has been claimed that pellagra existed in Southern prisons during the Civil War. The actual occurrence of the disease has not been completely established from contemporary records, but the assertion is made from memory by a physician, Dr. W. J. W. Kerr, still living, and is based upon his medical service at Andersonville (Ga.) prison.

Dr. H. N. Sloan, a former assistant physician, says the diagnosis of pellagra was made at the Lunatic Asylum, Columbia, S. C., in the early 70's. Contemporary records of the name have not yet been found, but I have no doubt that this claim is in all probability correct.

Dr. Samuel Sherwell, a dermatologist of Brooklyn, N. Y., reported cases of pellagra in 1882[11] and 1902.[12] These cases were in Italian sailors and therefore not indigenous. Another dermatologist, Van Harlingen, of Philadelphia, had written the warning in 1882 that pellagra was likely to occur at any time in this country.

Dr. D. S. Pope, of Columbia, S. C., now remembers that he saw two cases of probable pellagra in the State Penitentiary in this city

about 1885. He rejected his tentative diagnosis of pellagra, however, because the authorities stated that it did not exist in the United States. I know of other physicians also who have abandoned the diagnosis of pellagra out of respect to authority.

In 1889 Dr. Bemis left a written but unpublished diagnosis of pellagra for a case in the Charity Hospital of New Orleans. Drs. Wood and Bellamy, of Wilmington, N. C., have traced a case of pellagra back to 1889 in that State. Dr. J. J. Watson in 1895 saw in the Columbia, S. C., Almshouse what he now knows was a case of pellagra. Dr. T. P. Whaley, of Charleston, S. C., saw in that city in 1897 three cases of a condition which he called "pellagroid." These were among negroes from John's Island, a small island just a few miles off the coast below Charleston.

In 1902 Dr. H. F. Harris, of Georgia, reported[13] a case of anchylostomiasis with symptoms of pellagra, which was probably a case of pellagra associated with hookworm disease, but unfortunately he lost sight of the patient. Since reports of no other cases followed, it has been truly said[14] "The report of Dr. Harris excited but little comment."

In 1903 Dr. H. E. McConnell, of Chester, S. C., made the diagnosis of pellagra but unfortunately did not publish his observations. Furthermore, two general practitioners, one in North Carolina, Dr. J. E. Wright, of Lincolnton, and one in Alabama, referred to Dr. Isadore Dyer, of New Orleans, each diagnosed pellagra some years before its general recognition in those States.

In 1907 Dr. G. H. Searcey, of Alabama, published[15] an account of an epidemic of pellagra at the Mt. Vernon, Ala., Hospital for Colored Insane. As a result of this publication the report of one case was made by Dr. T. C. Merrill, of Texas.[16] At the meeting of the American Medical Association in 1907, Dr. E. J. Wood, of Wilmington, N. C., reported[17] several cases which he considered an unusual form of symmetrical gangrene probably of malarial origin. Subsequently Dr. Wood has classified these cases as pellagra. Dr. Wood's report was published in the same medical journal and in the same year as the reports of Dr. Searcy and of Dr. Merrill.

There is no doubt that, as has been its history in other countries, so in the United States, pellagra has been masked under many names, such as malaria, sprue, scurvy, etc. It will be recalled that having been observed in Egypt in 1847 by Pruner, pellagra was

altogether overlooked in that country and Pruner's diagnosis was questioned by Hirsch till the disease was rediscovered by Sandwith in 1893. Since then the prevalence of pellagra in Egypt has been well established by Sandwith, Warnock and others. Have we any reason to infer that it was absent from that country through nearly half a century? Moreover, in Manson's opinion:[18] "When once established in a district it (pellagra) remains there, but the degree of prevalence varies considerably from year to year."

Sambon says:[19] "Until quite recently all American textbooks stated quite emphatically that pellagra was unknown in that part of the world; then suddenly the disease is discovered in no fewer than twenty-six States and the absence of any definite history of recent importation or outbreak shows very clearly that the disease is of long standing in the United States, yet it escaped recognition."

In December, 1907, a report was made[20] to the South Carolina State Board of Health by the officers of the State Hospital for the Insane in Columbia upon nine cases of probable pellagra occurring in South Carolina and in that institution. This paper was given wide circulation in medical journals and newspapers and stimulated further investigation. Rosenau has written[21] that this report "aroused our present revival of interest in the disease." It will be recalled that Searcy's paper was followed by the report of one case by Merrill and that both of these were entirely overlooked by Wood, who regarded his cases of malarial origin.

In the summer of 1908 pellagra as seen in South Carolina was independently identified with Italian pellagra, as found near Milan, by Drs. J. J. Watson and J. W. Babcock, of Columbia, S. C. This identification removed some skepticism; but doubts of its existence in this country persisted and still persist in some quarters. During and after 1908 pellagra began to be recognized in many Southern States. As for the North and West, in 1909 it was diagnosed by Dr. L. I. Pollock at Cook County Hospital in Chicago, and by Dr. F. J. Griffin in the State Hospital at Peoria, Ill. In 1910 its presence was demonstrated by Dr. Samuel Stern in the Philadelphia (Blockley) Hospital. Stern's diagnosis was confirmed by J. D. Long and H. F. Harris. In the summer of 1910 Dr. Henry A. Jones recognized the first case of pellagra in Rhode Island at the State Institution at Howard, where up to the fall of 1912 twenty-seven cases of pellagra were discovered.

Since 1908 the area in which pellagra has been recognized in the United States has gradually enlarged, and the estimated numbers have correspondingly increased. In 1909, 1,000 cases were estimated in 16 States; in 1910, 3,000 cases in 31 States; in 1911, 20,000 cases in 37 States, and in 1912, 25,000 to 30,000 in 39 States. It is recalled that the estimate of 1,000 cases in 1909 was made doubtfully and with apprehensions of adverse criticism. Recently Dr. H. F. Harris, Health Officer of the Georgia State Board of Health, has estimated that there are 50,000 cases of pellagra in his State alone.

The disease, as noted by Roberts,[22] seems yet to be sporadic in the New England and Middle Atlantic States, epidemic in the Southern States, and sporadic again on the Pacific Coast. It should be noted that the western area from which pellagra has not been reported is that of the most sparsely populated portion of the United States. I am of opinion that pellagra prevails in many parts of this country to a much greater extent than is recognized or admitted. Of no disease can it be more truly said: We find what we look for.

Many difficulties lie in the way of discovering positive evidence of the early existence of pellagra in the United States. This striking paragraph is to be found in a recent government report.[23]

"Pellagra, a disease which has recently received considerable attention, caused 368 deaths in the registration area during the year 1910; for 1909 only 116 deaths from this cause were returned and for 1908 only 23; while the only deaths reported for previous years were 2 in 1900; 2 in 1903; and 1 in 1904. Although this disease has undoubtedly prevailed a long time in some portions of the United States, it has not been recognized or reported in this country until very recent years. For this reason the increase in the number of deaths reported cannot be regarded as representing an actual increase in the annual mortality."

Here seemingly we have five early cases—1900-1904—that have been overlooked by recent students of the history of pellagra in our country. Of the cases in 1900 one was from New Hampshire and one from New York. Of those of 1903, one was from New York and one from Illinois; and the one from 1904 was from Chicago.

In my efforts to get particulars of these cases this is what I have learned: Dr. Irving A. Watson, Secretary of the New Hampshire Board of Health, writes (July 26, 1912): "I am of the opinion that the statement in the Mortality Statistics 1910, Bureau of the

Census, that a case of pellagra was reported from New Hampshire in 1900, to be an error. We do not find such a record in this department. I am very certain that it must be a mistake." The Secretary of the Illinois State Board of Health, Dr. J. A. Egan, states (July 25, 1912): "The cases in question were never reported to the State Board of Health," and refers me to the authorities at Jacksonville and Chicago, cities from which the cases were reported. The Commissioner of the New York State Department of Health, Dr. E. H. Porter, writes (July 24, 1912): "I regret that no record was kept of the pellagra cases reported in the State of New York during the years 1900 and 1903, nor am I able to find any record of such cases."

In his careful notes on the epidemiology of pellagra in America Dr. R. M. Grimm[24] observes: "It would seem that the disease (pellagra) had been present here (in Kentucky and South Carolina) for a number of years," and he cites cases of pellagra whose history he has been able to trace back to dates before its general recognition: 1906, seven cases; 1905, five cases; 1904, six cases; 1903, three cases; 1902, one case; 1897 (?), one case; 1893 (?), two cases.

This presents an outline of the recorded and traditional history of pellagra in the United States. Is it not possible to fill in the details so as to make that history somewhat clearer and more distinct? Has not the disease been present in many of these States and cities and been overlooked? If overlooked, to what has the oversight been due? Has it been ignorance or prejudice or both? Retrospectively is it not possible for individuals to recall cases of the disease? Efforts in this direction have not been without results. Dr. I. M. Taylor traces it back at the Morganton (N. C.) State Hospital to 1887. In institutions in South Carolina, it is traced back to 1882 by persons now living, and in Georgia to 1884. Dr. Zeller, of the State Hospital at Peoria, Illinois, has established the presence of pellagra in that institution at least seven years prior to its recognition in 1909.

Dr. G. F. Gaumer, of Yucatan, Mexico, an authority on pellagra in that country, stated in a personal letter to me in 1911: "In April, 1893, I saw a case of pellagra in New Orleans. In May I recognized cases in Kansas City and from June to September I saw many cases in Chicago. And again in November on Williams and Chatham streets in New York. Most of the cases seen during the sum-

mer were Italians; several were American negroes and six cases in Cook County Hospital were white Americans. I have no doubt that pellagra has existed in the United States for many years." Since in the last five years pellagra has been observed in all these places, the correctness of Dr. Gaumer's earlier observations should not be denied without further investigation.

Of course, the careful observations of one individual are always valuable, but their value is increased when confirmed by other observers, acting separately and independently. Strikingly confirmatory and collateral evidence of Gaumer's observations of the existence of pellagra in the United States is to be found in Eden Paul's translation of Kurella's "Cesare Lombroso."[25] "Translator's Note: Dr. Kurella writes to me to the following effect: I remember twenty-five years ago in asylums both in Pennsylvania and in Illinois, finding cases of pellagra, with the characteristic skin lesions in addition to the mental disorders. But my American colleagues then ridiculed my diagnosis." These observations must have taken place in 1885. Recently pellagra has been observed, as noted above, in institutions both in Illinois and Pennsylvania. Dr. Bayard Holmes, of Chicago, has written:[26] "The older physicians of the country who now for the first time see named cases of pellagra collected together in the asylums and poorhouses, recall from the memory of the early years of their practice similar cases which they were never able to place in any nosological category." Dr. Holmes follows this statement with the history of a case of probable pellagra which William Brocksmith, M. D. (Berlin, Prussia, 1865), diagnosed as pellagra at Georgetown, Missouri, in 1882. The disease was called "corn scrofula" by the colored people of the neighborhood.

I am forced from personal experience and from facts related to me to believe that in some parts of the United States and in some institutions for the insane the diagnosis of pellagra is even today not sanctioned by the physicians in charge. I have demonstrated a case of pellagra to the asylum officer who had it in charge, but was not asked to extend my observations and I know that the presence of pellagra there was subsequently denied. I further know of at least one large asylum in which an assistant physician lost his position because of his persistence in making the diagnosis of pellagra, after being warned by his superiors not to do so, although his diagnosis was confirmed by two unusually competent men.

Dr. Rupert Blue, now Surgeon General of the United States Public Health Service, advanced the opinion in 1910 in an article on pellagra in California that pellagra could be found in nearly all the insane asylums and almshouses in this country. Whereas I formerly considered this statement too sweeping, I am now inclined to agree with it. In a recent study of the local medical history of South Carolina the writer, being physician to one of the oldest insane asylums in the country, has endeavored to trace the occurrence of pellagra from the records and case histories of the institution. He has satisfied himself that an obscure disease, always associated with insanity and intestinal disorders, has been prevalent in the hospital since is opening in 1828. The records show that this disease had been considered as scorbutic (early and recently); also as purpuric. Early diagnoses for such cases were "chronic diarrhœa" and "dysentery," which later gave place to "consumption," "inanition," and "marasmus;" and in the last two decades to "tuberculosis," "meningo-encephalitis" and "syphilis." Upon the evidence of persons now living, no possible doubt can exist as to the presence of the disease in this hospital for a generation or more. The most complete history, however, was found in a very early case-book. Briefly, the patient was admitted in February, 1834, suffering from a second attack of insanity. He was violent, homicidal and suicidal. Soon after admission he developed insomnia and severe diarrhœa. Ptyalism was noted. He emaciated and had exacerbations of diarrhœa, especially at night. In August the skin on the dorsa of his feet became of a sombre brown color, suggesting purpura. In September the purpuric rash involved his hands and scurvy was suspected. In October the diarrhœa, which had persisted in spite of treatment, is recorded as incorrigible at night. Later he became edematous and the "purpura" reappeared. In spite of an antiscorbutic dietary, his diarrhœa persisted, he became exhausted and expired on November 22, 1834. This case is identical with those occurring in this hospital and in this State for the last twenty or thirty years. The conclusion is therefore reached that pellagra is not a new disease in South Carolina. This opinion is concurred in by other American pellagrologists. The published monograph of my former study of local medical history was sent to a number of authors and professors. A few opinions may be cited:

In commenting upon it Sir William Osler, Regius Professor of Medicine, Oxford, England, has written (9th July, 1912): "That is a most interesting historical note of yours on pellagra. It leaves precious little doubt that the disease must have existed many years in the South. Strange that there is not more of it seen in England. I have been on the watch lately."

Dr. C. C. Bass, Associate Professor of Tropical Diseases in Tulane University, New Orleans, has thus commented: "I quite agree with you that in all probability pellagra has been here for at least fifty or one hundred years. I go still further than you and question whether there is any more pellagra today in the United Sates than there was twenty years ago, except for such changes in numbers as would result from migration, emigration and increase of population. The more I learn of the disease, the more certain I feel that it is not a new disease in this country."

From this imperfect preliminary sketch some conclusions may be drawn:

Pellagra was recorded in 1864 as having been observed in New York and Massachusetts. As today cases of the disease are known to exist in both of those States, the early diagnoses of the disease made by very competent alienists were probably correct.

In view of the recognition of pellagra in Missouri asylums in 1910, we are not justified in doubting the diagnosis made in 1882 by Dr. Brocksmith. Kurella says his diagnosis of pellagra in asylums in Illinois and Pennsylvania was ridiculed in 1885. Gaumer independently claims to have seen cases of the disease in Illinois in 1893 and it was recognized there in 1909 and in Pennsylvania in 1910. Shall not the earlier diagnoses stand now?

In all the other States in which Gaumer claims to have seen cases of pellagra in 1893 the disease has recently been observed. Are not his early observations trustworthy evidence? We cannot deny the correctness of Harris's and McConnell's observations of a decade ago. In the seemingly long intervals of silence upon the subject have we a right to say that the disease had disappeared and that the correct diagnosis was made for all cases as they occurred or developed? Or shall we admit the continuity of its existence?

My own studies of pellagra cases have been confined largely to one State and to one insane asylum. From the written and printed records of this institution, however, I have satisfied myself and

others familiar with the disease that pellagra has probably been present in South Carolina at least since 1828 and that its presence has practically been continuous.

If such evidence has been discovered by one isolated investigator it is more than probable that research in other hospitals and certainly in adjoining States will disclose similar records and evidence.

Evidence is therefore accumulating that pellagra is by no means a new disease in the United States. It has already been traced back in several States to various earlier periods.

For example:

In South Carolina	1828
In Massachusetts	1860
In New York	1863
In Missouri	1882
In Georgia	1884
In Illinois	1885
In Pennsylvania	1885
In North Carolina	1887
In Louisiana	1889

These dates are, of course, tentative, serving merely as starting points in our medical history. The prior existence of pellagra in the several localities can yet neither be affirmed nor denied, but further inquiry may and probably will extend these limits both as regards time and place.

This imperfect sketch establishes, I think, the early existence of pellagra in the United States. The present widespread and, in some places, excessive prevalence of the disease hardly comes within the scope of this inquiry. This part of the problem is now being studied with much zeal by many competent men throughout the United States. Many corroborative details are needed to complete the history. These will no doubt follow from students of the disease and of the history of medicine.

In conclusion, I wish to thank the charter members of this Association for the high honor of electing me its first president. Since our last meeting much good work has been done in the United States in the observation of facts concerning pellagra. Like our European confreres we appear to be dividing into the two camps of zeist and antizeist. So long, however, as we remain open-minded and tol-

erant, seeking truth for its own sake and not biased or guided by sentiment or by less worthy motives, we shall each contribute his modicum towards solving the great and many-sided problem of the cause of pellagra. I thank you—new members and old—most heartily for your presence here today and bid you and the public, too, welcome to our deliberations. We will now proceed to the regular business announced on the exceedingly interesting program that has been prepared for you.

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II. Etiology, Epidermiology and Statistics of Pellagra

THE PREVALENCE AND GEOGRAPHIC DISTRIBUTION OF PELLAGRA IN THE UNITED STATES.

By C. H. LAVINDER, Surgeon, United States Public Health Service.

Ever since the recognition of pellagra as a disease endemic and prevalent in the United States various attempts have been made to determine with some degree of exactitude its prevalence and geographic distribution, but up to the present time this very important information is still wanting, and we have been compelled to depend upon estimates which have not always been based upon any very accurate data. Under the direction of the Surgeon General of the Public Health Service I began some time ago a systematic attempt to collect statistical information relative to this disease in the United States. This work has proceeded slowly and suffered many interruptions, and my record is as yet by no means complete. I believe, however, that with the data I now have and the information compiled by others we are in a position when for the first time we may say with some degree of assurance approximately how much pellagra we have had in the United States and where it is prevailing. My report, as stated, is incomplete and must be taken as preliminary to a fuller report, which it is my hope may be made at no very distant date, when the work of collecting data is completed and the results compiled.

The pellagrous area of the United States lies, to a large extent, outside of the "registration area" for deaths as defined by the Census Bureau, and the statistics on this disease furnished by the Census Bureau are really almost a negligible quantity. In compiling data, therefore, we are compelled to depend upon reports made by individuals, and upon personal appeals, by card or letter, to State health officials, superintendents of asylums for the insane, heads of public institutions, and individual practitioners. It is needless to say that this method is faulty, and the resulting information by no means as accurate or complete as one would wish. The appeal to

State health officials is of little value, since the disease is reportable in but very few States, and in only one of them by law. There are very few statistical reports in existence, and such as do exist have also been compiled with these same faulty methods. Personal appeals by card or letter to individual practitioners and to public institutions generally, receive scant attention on the part of many; and in my experience, as I will show later, we have received replies to about one-fourth of the cards and letters sent out. The collection of statistical data on any very large scale is always necessarily open to many sources of error, however, and in the present case, notwithstanding faulty methods, I believe the returns give us a fairly accurate idea of the extent and prevalence of pellagra in the United States.

I have collected information from eight of the principal States of the pellagrous area by means of a franked return postal card, sent to each individual practitioner in these States. The report side of the return card is shown by the following:

REPORT SIDE OF RETURN CARD SENT TO PHYSICIANS.

PELLAGRA.

How many cases of pellagra occurred in your practice during 1907?.....; 1908? .....; 1909? .....; 1910? .....; 1911? ..... Total cases, ...; total deaths, ... How many in white males? .....; white females? .....; colored males? .....; colored females? ..... How many under 5 years of age? .....; 5 to 20? .....; 20 to 40? .....; above 40? ..... How many were city people? .....; country people? .....; well to do? .....; moderate circumstances? .....; poor? ..... How many times have you observed in one family or one house more than one case? .....; more than two cases? .....

Remarks: .....

Date, ...

(Signature).....,

(Address) .....

Especial attention is directed to the fact that in this reply card note is taken only of the calendar years 1907 to 1911, both inclusive. These years are taken for the reasons that pellagra was first recognized as prevailing in the United States in the latter part of 1906 and early part of 1907, and my inquiry was begun comparatively early in 1912. The information derived from the cards sent to individual practitioners in the eight States mentioned above is shown partially in Table 1. The details of the inquiry will be shown

in subsequent tables and charts. For all other States I have been compelled to rely upon personal correspondence, reports of various kinds, and miscellaneous information derived in many ways. Some of the information which has been collected has as yet not been compiled, but such as has been is given in detail in the subsequent tables and charts.

TABLE No. 1.—*Pellagra, 1907 to 1911, inclusive.*

States.	Reports.		Race and Sex of Reported Cases.				Race and Sex Not Reported.	Total Cases.	Deaths.	Death Rate per 100 Reported Cases.
			White.		Colored.					
	Replies.	Cards Mailed.	Male.	Female.	Male.	Female.				
Virginia	2,350	823	174	302	49	103	.....	628	349	55.59
North Carolina	1,849	521	543	1,201	130	277	261	2,412	1,067	44.37
South Carolina	1,275	287	357	772	120	351	280	1,880	582	30.95
Georgia	3,022	735	985	2,149	166	575	690	4,558	1,582	34.70
Kentucky	3,601	723	159	283	15	24	32	513	220	42.88
Alabama	2,418	561	150	988	133	680	363	2,314	859	37.12
Mississippi	2,009	561	433	954	249	907	352	2,895	1,250	43.17
Louisiana	1,930	446	123	215	69	200	63	670	296	44.17
Total	18,463	4,657	2,924	6,857	931	3,117	2,041	15,870	6,205	[1]39.01

The figures in Table No. 1 do not include reports from the insane asylums in these States. I have excluded these for the reason that I found it impossible to determine with any degree of exactitude what percentage of cases developed in the asylums and what percentage were sent in already pellagrous. Undoubtedly many cases of pellagra have developed in the insane asylums of these States, but since I could not determine what percentage of the total did so develop, to have included them would have meant duplicating perhaps the reports already received from individual practitioners, many of whose cases have ultimately found their way into the asylums.

It will be noted in this table that I have received replies to only about 25 per cent. of the cards sent out. It is, of course, questionable just what this may mean, and at first I was inclined to think that perhaps no reply might simply mean that the physician had no cases to report. Later developments and further experience, however, have taught me that this is by no means true. I believe that

[1]Aggregate fatality rate per 100 reported cases.

the absence of replies to so many cards means a great many unreported cases, but just how many no one can say.

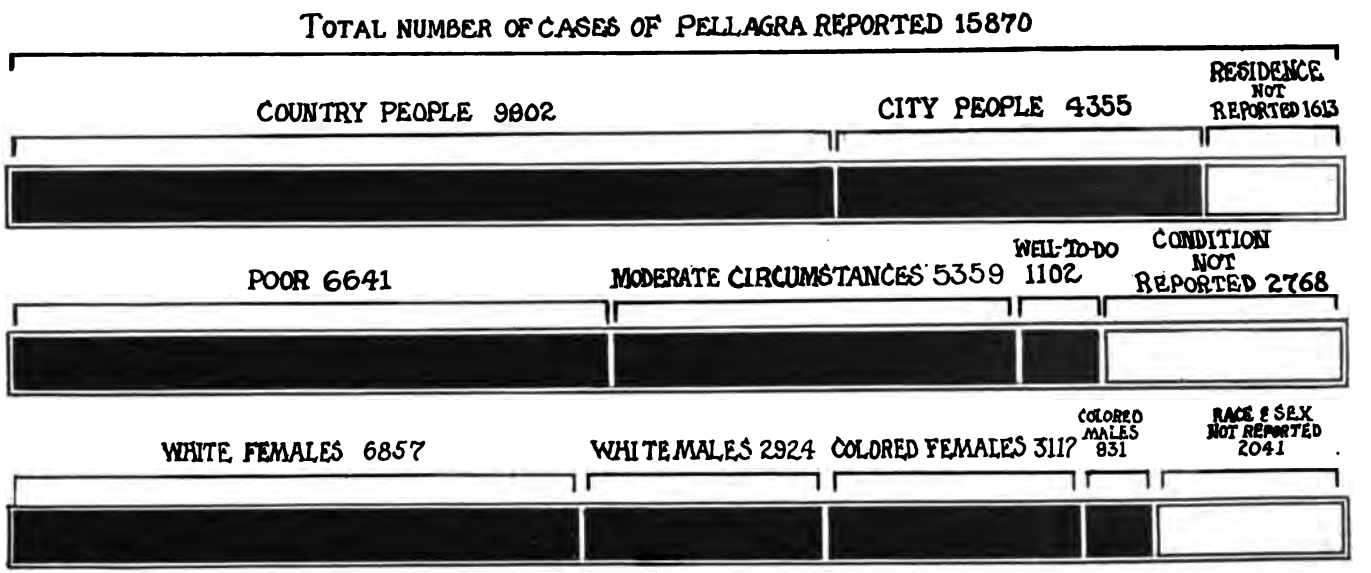
Attention is directed to the very high case fatality rate, and it may be pointed out that this rate is among nonasylum cases. If we should add to this the deaths in the insane asylums in these States I am satisfied that the average case fatality rate would be higher. The death rate among asylum cases is very heavy.

The details as to race and sex are shown graphically in the chart which follows, Chart No. 1, as are also certain other data. In this chart it is of especial interest to notice the ratio between the whites and negroes, both male and female. It has been thought by many that in the South negro females have been the worst sufferers from pellagra. But here in a total of nearly 14,000 cases, reported from States many of which have a large negro population, we find that the white females outnumber the negro females and the white males outnumber the negro males. This shows the folly of trying to make generalizations on a small number of cases, as has been done heretofore.

The rural cases, as seen in this chart, exceed the urban cases, though the latter occur in large numbers. This is totally at variance with Italian pellagra, which is not found in the cities at all. It may be said, however, that there is room for wide latitude in answering such questions as, "How many were city people?" or "How many were country people?" The conditions of life in small villages and towns are not infrequently rural rather than urban. And it is more than likely that many of the cases reported here as in the city, may have occurred in towns or villages of this character. From this same chart it is noted that the disease is reported more frequently among the poor and those in moderate circumstances, but does not spare the well-to-do. This is quite in keeping with the Italian disease of which Dalla Bona said: "It does not always spare the palace."

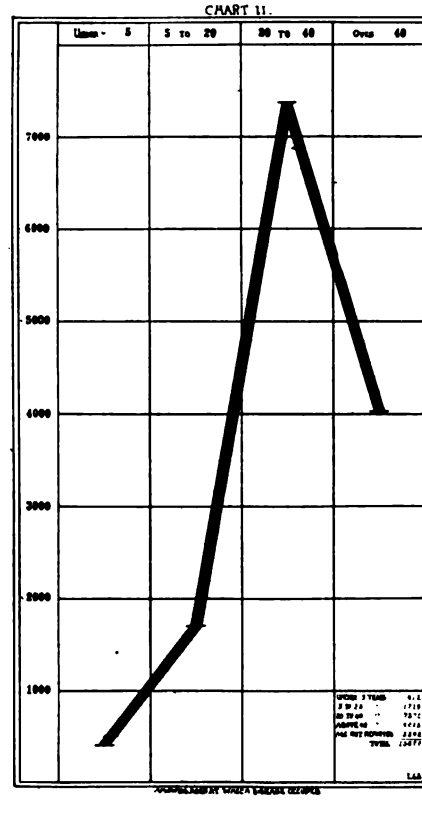
The information derived from the question as to whether there were more than one or two cases in a house or family is perhaps worthy of little notice since it gives little that is definite. However, from a tabulation of the answers it appears that more than one case was noted 933 times, and more than two cases 235 times, that is, in the total reported cases, nearly 16,000 in number. So far as it goes, this is in entire accord with the Italian observations. There, as

CHART I.



FROM THE ANALYSIS OF THE TOTAL CASES REPORTED FROM EIGHT STATES-1907 TO 1911 INCLUSIVE

CHART 11.


Under 5
5 to 20
20 to 40
Over 40
7000
6000
5000
4000
3000
2000
1000

here, it is much more frequently observed that there is only one case in a house or family. This is perhaps a point of some consequence regarding the transmissibility of the disease.

In Chart No. 2 is shown graphically the time of life when the disease occurred in all of the cases in which this information is given. This curve would have been of much more interest had the groups been in five-year periods or less, but the collection of so much detail was not found feasible.

In Table No. 2, I have tried to give an estimate of the total cases which have occurred in the United States during the calendar years 1907 to 1911, inclusive.

TABLE No. 2.—*Showing estimated total number of cases of Pellagra in the United States, 1907 to 1911, inclusive.*

Eight States:	
Reported	15,870
Not reported (estimated)	4,000
Maryland	25
Tennessee	2,500
Florida	250
Arkansas	500
Texas	1,500
Illinois and Pennsylvania	700
All other States	200
Total	25,545

This table is not based on actual figures throughout, but has been compiled from all the data available, and while doubtless containing errors, it is nevertheless, in my opinion, a very conservative statement. If we presume, as I think we safely may, that the disease is still increasing during the present year, then with this total of 25,545 cases up to the end of 1911 we may certainly say that up to the present time there have occurred a total of not less than 30,000 cases of pellagra in the United States since the recognition of this disease as endemic and prevalent in this country. Indeed, I think we might very safely increase this total and still remain well within the limits of truth.

In the large map of the United States I have tried to show in a general way the distribution of pellagra in the United States. Such a map can give only a general idea of the prevalence of the disease, but it serves to show and emphasize this very well. It is to be noted

that there are nine States which have not as yet reported the disease. These are New Hampshire in the New England States, and all the others are grouped together in the North and West: Idaho, Minnesota, Montana, North and South Dakota, Utah, Wyoming and Nevada.

The following table, No. 3, which shows the number of cases reported in each county in the States for which detailed information was obtained, will serve in some measure to show the distribution of the disease in these eight States. These data were compiled some time ago, and do not include a few cases reported since. The totals therefrom will be somewhat less than the totals given in Tables 1 and 2.

TABLE No. 3.—*Showing by counties the number of cases of Pellagra reported in Alabama, Georgia, Kentucky, Louisiana, Mississippi, North Carolina, South Carolina and Virginia.*

Counties.	Cases.	Counties.	Cases.
ALABAMA.		ALABAMA—*Continued.*	
Autagua	4	Fayette	12
Baldwin	17	Franklin	8
Barbour	41	Geneva	13
Bibb	50	Greene	28
Blount	39	Hale	30
Bullock	26	Henry	...
Butler	36	Houston	18
Calhoun	63	Jackson	28
Chambers	12	Jefferson	225
Cherokee	3	Lamar	24
Chilton	43	Lauderdale	13
Choctaw	34	Lawrence	28
Clarke	155	Lee	31
Clay	12	Limestone	5
Cleburne	7	Lowndes	28
Coffee	...	Macon	33
Colbert	13	Madison	6
Conecuh	3	Marengo	61
Coosa	17	Marion	15
Covington	11	Marshall	70
Crenshaw	9	Mobile	41
Cullman	27	Monroe	10
Dale	21	Montgomery	126
Dallas	80	Morgan	68
Dekalb	23	Perry	23
Elmore	25	Pickens	37
Escambia	12	Pike	47
Etowah	79	Randolph	39

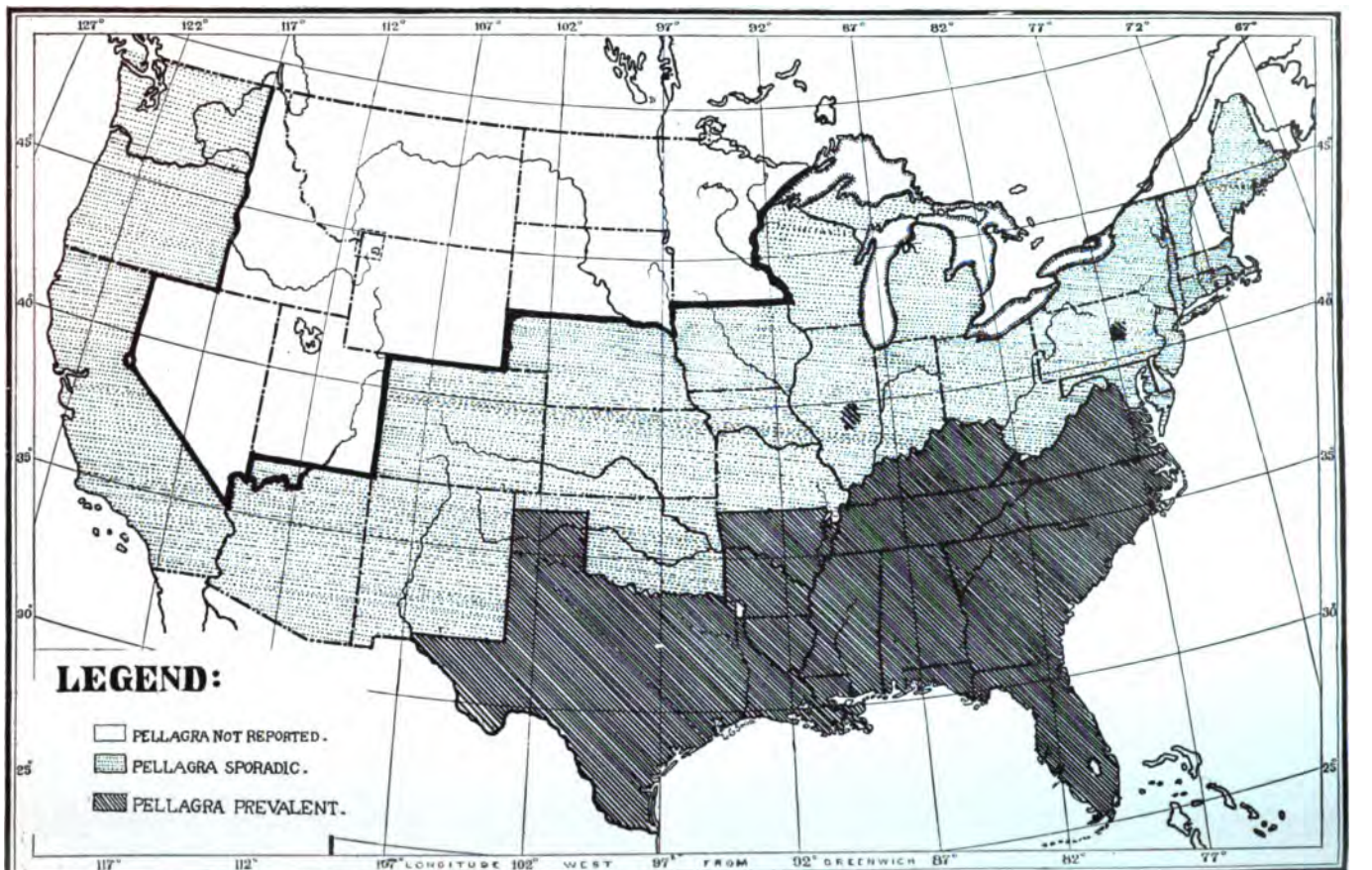

LEGEND:
PELLAGRA NOT REPORTED.
PELLAGRA SPORADIC.
PELLAGRA PREVALENT.
LONGITUDE WEST FROM GREENWICH

TABLE No. 3.—*Showing by counties the number of cases of Pellagra reported in Alabama, Georgia, Kentucky, Louisiana, Mississippi, North Carolina, South Carolina and Virginia*—Continued.

Counties.	Cases.	Counties.	Cases.
ALABAMA—*Continued.*		GEORGIA—*Continued.*	
Russell	31	Dodge	6
Shelby	21	Dooly	6
St. Clair	15	Dougherty	22
Sumter	40	Douglas	24
Talladega	62	Early	2
Tallapoosa	9	Echols	...
Tuscaloosa	61	Effingham	12
Walker	63	Elbert	21
Washington	29	Emanuel	6
Wilcox	92	Fannin	7
Winston	12	Fayette	10
		Floyd	145
GEORGIA.		Forsyth	9
		Franklin	33
Appling	3	Fulton	862
Baker	1	Gilmer	...
Baldwin	25	Glascock	4
Banks	14	Glynn	4
Bartow	91	Gordon	45
Ben Hill	48	Grady	8
Berrien	14	Greene	37
Bibb	104	Gwinnett	111
Brooks	15	Habersham	99
Bryan	4	Hall	95
Bulloch	4	Hancock	2
Burke	6	Haralson	11
Calhoun	11	Harris	9
Camden	16	Hart	21
Campbell	29	Heard	30
Carroll	47	Henry	59
Catoosa	...	Houston	19
Chatham	61	Irwin	3
Chattooga	5	Jackson	104
Cherokee	25	Jasper	9
Clarke	66	Jeff Davis	10
Clay	4	Jefferson	14
Clayton	72	Jenkins	3
Clinch	3	Jones	8
Cobb	113	Laurens	16
Coffee	29	Lee	8
Colquitt	41	Liberty	2
Columbia	9	Lincoln	7
Coweta	78	Lowndes	21
Crawford	8	McDuffie	3
Crisp	21	McIntosh	2
Decatur	8	Macon	14
Dekalb	126	Madison	5

TABLE No. 3.—*Showing by counties the number of cases of Pellagra reported in Alabama, Georgia, Kentucky, Louisiana, Mississippi, North Carolina, South Carolina and Virginia*—Continued.

Counties.	Cases.	Counties.	Cases.
GEORGIA—*Continued.*		GEORGIA—*Continued.*	
Marion	9	Wayne	9
Meriwether	51	Webster	4
Miller	4	White	6
Milton	14	Whitfield	109
Mitchell	...	Wilcox	25
Monroe	39	Wilkes	9
Montgomery	18	Wilkinson	4
Morgan	16	Worth	16
Murray	4		
Muscogee	105	KENTUCKY.	
Newton	33		
Oconee	9	Adair	...
Oglethorpe	1	Allen	2
Paulding	20	Anderson	...
Pickens	31	Ballard	...
Pierce	5	Barren	1
Pike	19	Bath	1
Polk	87	Bell	47
Pulaski	15	Boone	...
Putnam	9	Bourbon	1
Quitman	36	Boyd	1
Rabun	4	Boyle	2
Randolph	35	Bracken	...
Richmond	104	Breathitt	4
Rockdale	23	Breckenridge	...
Screven	6	Bullitt	...
Spalding	93	Butler	...
Stephens	55	Caldwell	...
Stewart	13	Calloway	5
Sumter	25	Campbell	1
Talbot	10	Carroll	1
Taliaferro	19	Carter	18
Tattnall	...	Casey	1
Telfair	6	Christian	...
Terrell	54	Clark	1
Thomas	22	Clay	2
Tift	7	Clinton	...
Toombs	28	Crittenden	...
Troup	68	Cumberland	...
Turner	...	Daviess	2
Twiggs	1	Elliott	...
Union	5	Estill	...
Walker	60	Fayette	57
Walton	7	Fleming	1
Ware	53	Floyd	...
Warren	22	Fulton	...
Washington	24	Gallatin	...

TABLE No. 3.—*Showing by counties the number of cases of Pellagra reported in Alabama, Georgia, Kentucky, Louisiana, Mississippi, North Carolina, South Carolina and Virginia*—Continued.

Counties.	Cases.	Counties.	Cases.
KENTUCKY—*Continued.*		KENTUCKY—*Continued.*	
Garrard	12	Nelson	32
Grant	...	Nicholas	...
Graves	1	Ohio	2
Grayson	2	Oldham	...
Green	...	Owen	...
Greenup	...	Owsley	...
Hancock	...	Pendleton	...
Hardin	...	Perry	...
Harlan	...	Pike	2
Harrison	...	Powell	3
Hart	6	Pulaski	1
Henderson	...	Robertson	...
Henry	...	Rockcastle	2
Hickman	...	Rowan	...
Hopkins	4	Russell	1
Jackson	...	Scott	...
Jefferson	97	Shelby	...
Jessamine	2	Simpson	...
Johnson	1	Spencer	...
Kenton	..	Taylor	5
Knox	52	Todd	5
Larue	...	Trigg	...
Laurel	19	Trimble	...
Lawrence	1	Union	3
Lee	...	Warren	5
Letcher	2	Washington	3
Lewis	...	Wayne	2
Lincoln	1	Webster	1
Livingston	...	Whitley	39
Logan	...	Woodford	1
Lyon	3		
McCracken	6	LOUISIANA.	
McLean	2		
Madison	1	Acadia	4
Magoffin	...	Ascension	7
Marion	...	Assumption	4
Marshall	1	Avoyelles	4
Martin	14	Bienville	4
Mason	...	Bossier	9
Meade	...	Caddo	46
Menifee	...	Calcasieu	30
Mercer	...	Caldwell	2
Metcalfe	...	Catahoula	5
Monroe	2	Claiborne	23
Montgomery	...	Concordia	5
Morgan	...	De Soto	34
Muhlenberg	...	East Baton Rouge	27

TABLE No. 3.—*Showing by counties the number of cases of Pellagra reported in Alabama, Georgia, Kentucky, Louisiana, Mississippi, North Carolina, South Carolina and Virginia*—Continued.

Counties.	Cases.	Counties.	Cases.
LOUISIANA—*Continued.*		MISSISSIPPI.	
East Carroll	15	Adams	83
East Feliciana	12	Alcorn	29
Franklin	4	Amite	55
Grant	14	Attila	27
Iberia	6	Benton	...
Iberville	7	Bolivar	71
Jackson	31	Calhoun	10
Jefferson	...	Carroll	9
Lafayette	1	Chickasaw	95
Lafourche	4	Choctaw	27
La Salle	4	Claiborne	3
Lincoln	10	Clarke	26
Livingston	2	Clay	35
Madison	1	Coahoma	77
Morehouse	4	Copiah	10
Natchitoches	14	Covington	59
Orleans	62	De Soto	76
Ouachita	12	Forrest	39
Plaquemines	1	Franklin	3
Pointe Coupee	2	George	3
Rapides	11	Greene	2
Red River	...	Hancock	...
Richland	2	Harrison	87
Sabine	5	Hinds	114
St. Bernard	...	Holmes	54
St. Charles	1	Issaquena	...
St. Helena	6	Ittawamba	14
St. James	1	Jackson	1
St. Landry	7	Jasper	42
St. Martin	3	Jefferson	8
St. Mary	18	Jefferson Davis	...
St. Tammany	7	Jones	15
Tangipohoa	52	Kemper	28
Tensas	9	Lafayette	26
Terrebonne	2	Lamar	7
Union	6	Lauderdale	307
Vermilion	3	Lawrence	64
Vernon	11	Leake	4
Washington	11	Lee	105
Webster	19	Leflore	45
West Baton Rouge	3	Lincoln	14
West Feliciana	...	Lowndes	33
Winn	56	Madison	9

TABLE No. 3.—*Showing by counties the number of cases of Pellagra reported in Alabama, Georgia, Kentucky, Louisiana, Mississippi, North Carolina, South Carolina and Virginia*—Continued.

Counties.	Cases.
MISSISSIPPI—*Continued.*	
Marion	9
Marshall	23
Monroe	177
Montgomery	37
Neshoba	36
Newton	8
Noxubee	12
Oktibbena	45
Panola	53
Pearl River	12
Perry	11
Pike	84
Quitman	4
Rankin	57
Scott	13
Sharkey	17
Simpson	30
Smith	2
Sunflower	56
Tallahatchie	23
Tate	31
Tippah	14
Tishomingo	12
Tunica	26
Union	37
Warren	...
Washington	126
Wayne	4
Webster	8
Wilkinson	18
Winston	32
Yalobusha	29
Yazoo	38
NORTH CAROLINA.	
Alamance	26
Alexander	2
Anson	67
Ashe	...
Avery	11
Beaufort	27
Bladen	3
Buncombe	173
Burke	26
Cabarrus	4
Caldwell	6

Counties.	Cases.
NORTH CAROLINA—*Continued.*	
Camden	...
Carteret	5
Caswell	1
Catawba	16
Chatham	27
Cherokee	20
Chowan	5
Cleveland	15
Columbus	12
Craven	39
Cumberland	180
Currituck	2
Dare	...
Davidson	5
Davie	9
Duplin	2
Durham	253
Edgecombe	4
Forsyth	39
Franklin	80
Gaston	20
Gates	...
Granville	17
Greene	8
Guilford	207
Halifax	11
Harnett	30
Haywood	25
Henderson	21
Hertford	2
Hoke	...
Iredell	5
Jackson	13
Johnston	34
Jones	2
Lee	8
Lenoir	7
Lincoln	21
McDowell	27
Macon	4
Madison	2
Martin	...
Mecklenburg	156
Mitchell	...
Montgomery	3
Moore	28
Nash	6

TABLE No. 8.—*Showing by counties the number of cases of Pellagra reported in Alabama, Georgia, Kentucky, Louisiana, Mississippi, North Carolina, South Carolina and Virginia.*—Continued.

Counties.	Cases.
NORTH CAROLINA—*Continued.*	
New Hanover	21
Northampton	2
Onslow	8
Orange	18
Pamlico	2
Pasquotank	8
Pender	45
Person	5
Pitt	33
Polk	14
Randolph	44
Richmond	25
Robeson	104
Rockingham	35
Rowan	62
Rutherford	32
Sampson	9
Scotland	3
Stanly	1
Stokes	6
Surry	15
Swain	...
Transylvania	...
Tyrrell	2
Union	24
Vance	22
Wake	77
Warren	27
Washington	2
Watauga	...
Wayne	18
Wilkes	5
Wilson	2
Yadkin	...
Yancey	1
SOUTH CAROLINA.	
Abbeville	17
Aiken	106
Anderson	131
Bamberg	10
Barnwell	6
Beaufort	39
Berkeley	22
Calhoun	2
Charleston	73
SOUTH CAROLINA—*Continued.*	
Cherokee	33
Chester	26
Chesterfield	7
Clarendon	8
Colleton	5
Darlington	19
Dillon	33
Dorchester	9
Edgefield	22
Fairfield	57
Florence	18
Georgetown	16
Greenville	145
Greenwood	98
Hampton	8
Horry	23
Kershaw	16
Lancaster	18
Laurens	95
Lee	10
Lexington	7
Marion	11
Marlboro	21
Newberry	35
Oconee	80
Orangeburg	53
Pickens	93
Richland	51
Saluda	11
Spartanburg	226
Sumter	37
Union	92
Williamsburg	12
York	25
VIRGINIA.	
Accomac	9
Albemarle	10
Alexandria	1
Alleghany	1
Amelia	1
Amherst	7
Augusta	17
Bath	...
Bedford	11
Bland	...

TABLE No. 3.—*Showing by counties the number of cases of Pellagra reported in Alabama, Georgia, Kentucky, Louisiana, Mississippi, North Carolina, South Carolina and Virginia.*—Concluded.

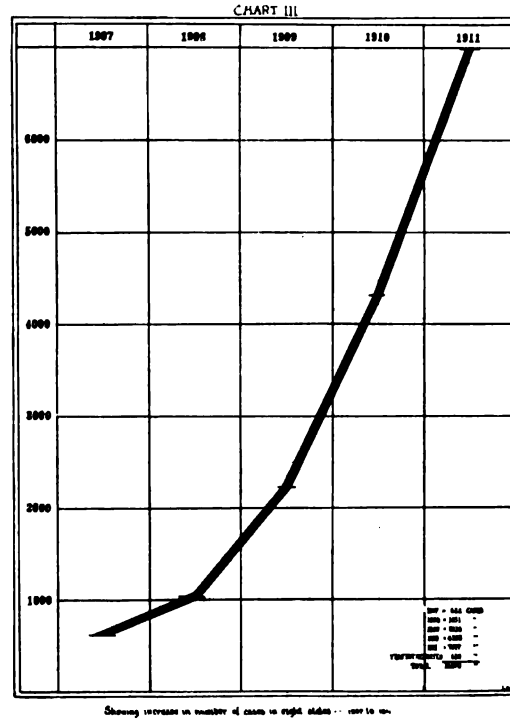
Counties.	Cases.	Counties.	Cases.
VIRGINIA—*Continued.*		VIRGINIA—*Continued.*	
Botetourt	2	Madison	1
Brunswick	4	Mecklenburg	12
Buchanan	1	Middlesex	1
Buckingham	1	Montgomery	13
Campbell	33	Nansemond	2
Caroline	...	Nelson	4
Carroll	...	Norfolk	64
Charles City	3	Northampton	2
Charlotte	5	Northumberland	2
Chesterfield	3	Nottoway	13
Clarke	...	Orange	3
Culpeper	2	Page	...
Cumberland	2	Patrick	1
Dickenson	...	Pittsylvania	39
Dinwiddie	8	Powhatan	3
Essex	...	Prince Edward	...
Fairfax	3	Prince George	4
Fauquier	13	Princess Anne	5
Floyd	2	Prince William	6
Fluvanna	1	Pulaski	2
Franklin	...	Rappahannock	...
Frederick	...	Richmond	2
Giles	1	Roanoke	31
Gloucester	...	Rockbridge	3
Goochland	2	Rockingham	6
Grayson	1	Russell	...
Greene	...	Scott	2
Greenesville	21	Shenandoah	2
Halifax	16	Smyth	8
Hanover	10	Southampton	12
Henrico	79	Spotsylvania	1
Henry	12	Stafford	12
Highland	...	Surry	...
Isle of Wight	11	Sussex	10
James City	22	Tazewell	5
King and Queen	...	Warren	1
King William	1	Warwick	4
Lancaster	...	Washington	4
Lee	7	Westmoreland	3
Loudoun	2	Wise	1
Louisa	4	Wythe	2
Lunenburg	2	York	2

Here, again, we are likely to receive wrong impressions unless Table No. 3 is studied with the conditions and circumstances well in mind. For example, it will be noticed in Georgia that Fulton county shows a large number of cases; but Atlanta is located in this county and a great many cases of the disease are sent into Atlanta for treatment. This probably accounts for many of the cases attributed to this county. A similar state of affairs is true for other places. Again, in South Carolina, Spartanburg county reports a large number of cases. This is due, partially, at least, to the fact that the profession in this county have taken a marked interest in the disease. They are therefore good diagnosticians and also make reports. A similar condition of affairs will be found in other places in these States. So that the geographical distribution as shown by this table can be accepted only in a general way.

The next chart, Chart No. 3, shows the increase in cases, by years, as reported from the eight States mentioned. The interpretation of this chart is also not without difficulty, and it is impossible to say just how much this rapid increase may be due to the spread of knowledge regarding the disease and increased skill in diagnosis among the profession. From my observation and experience I have no doubt that such factors may account for some of it, but I am equally convinced that it represents in large measure an actual increase in cases. I have collected figures only up to and including 1911, and so cannot say what may have happened during the present year of 1912; but so far as I can learn the disease is still spreading and increasing in numbers in practically all parts of the involved territory.

In concluding this paper I may say that no one can feel more dissatisfaction than myself concerning the want of greater accuracy in the figures presented. I feel justified, however, in presenting as I have the results of my inquiry since there exists no hope of our soon obtaining anything better. And whatever else may be charged against such a report I do not think any person at all conversant with the situation can say that I have in any manner exaggerated the existing condition of things. On the contrary, I feel sure that where I have erred it has been in statements too temperate rather than otherwise. I may point out here also, as has been done by Surg. Gen. Blue elsewhere, that, strictly speaking, it is not the proper function of the Public Health Service to collect these data, and in

CHART III



Showing increase in number of cases in eight states -- 1907 to 1911

so doing we have, perforce, gathered information which, under proper conditions, could have been supplied with greater ease and accuracy by the State health authorities. It is greatly to be hoped that this disease may be made reportable in the various States and the way opened for the collection of extensive and accurate data on the prevalence of such an important malady.

Numerically pellagra can not, of course, be compared with such a disease as typhoid fever, for example; but when consideration is given to the facts that a disease which was unknown to us some five to six years ago has within this brief period claimed not less than 30,000 victims with a case fatality rate in excess of 39 per cent., and which apparently is continuing its spread over wider territory with a constant increase in the numbers involved, then, I think, it may be safely said that this matter has reached the dignity of a public-health question of national importance.[1]

[1]In the preparation of this paper I am especially indebted to Pharmacist L. G. Smith, Public Health Service, who has collected most of the data and has prepared a large part of the tables, charts and maps.

PELLAGRA: SOME FACTS IN ITS EPIDEMIOLOGY.

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The purpose of this article is to present a few facts in the epidemiology of pellagra. These facts pertain to 323 cases of pellagra which were seen by me during the summers of 1911 and 1912 while engaged in the pellagra field-work undertaken by the United States Public Health Service. The object of this field-work was primarily to collect data which would show the character of the home environment of the pellagrins and the nature of the conditions under which the disease was developing; in short, to make a study of the disease from the standpoint of hygiene. It was thought that information bearing on these points, in a large series of cases, might be of some value in indicating a direction for some line of investigation which might possibly lead toward the discovery of the cause of the disease, or of a method of its transmission. With these points in view the facts in this article were collected and have been recorded here, with the hope that they may be of some interest now and of some value in the future, when supplemented by data from other sources.

During the progress of my work 200 or more physicians of Kentucky, South Carolina and Georgia were consulted, 296 pellagrous homes visited, and 323 pellagrins personally interviewed. The visits to the homes of the pellagrins were always made in company with the family physician. This rule was strictly adhered to. For collecting the data case-cards measuring 5 by 8 inches were used. These cards were numbered serially and are now on file. On the cards are spaces for notes pertaining to the following points: name, address, race, sex, age, nativity, marital condition, occupation, family history, personal and pellagrous history; date and place of onset of first and of subsequent attacks; number and health of other members of the family; relation to other cases, and any facts bearing on heredity and contagion. In each instance an attempt was made to get some idea of the character and source of the food and water which had been used in the families. During the visits to the homes of the pellagrins notes were taken on the economic condition of the families and on the sanitary condition of the houses and premises.

The relation of the homes to water-courses was noted, and also any other fact or circumstance which at the time seemed pertinent. On slight consideration it will be readily realized how many questions might be asked and what confusion of detail is possible, so that it was only between certain limits that the facts have been collected which I have attempted to put into communicable form in this article.

Geography, Topography, Etc.—During my work visits were made to districts in twenty-five counties in which pellagra had been reported prevalent—three in Kentucky, seven in South Carolina, and fifteen in Georgia. The Kentucky counties visited are located in the southeastern portion of the State, which is a mountainous coal mining section. The other counties are located in the northern, the western, and the southern portions of South Carolina and Georgia and belong to the rich agricultural sections of these States. The main industries there are the growing and the weaving of cotton, but considerable attention is also paid to the cultivation of corn. The elevation of the counties visited varies from about 1,000 feet above sea level in Kentucky and north Georgia down to almost sea level in the southern portion of the latter State. Cases of pellagra were found to have developed at practically every elevation between these limits, but more cases were seen in the rolling upland sections than in either the mountainous or low country All of these counties are well watered and possess good natural drainage, as is indicated by the presence of numerous streams flowing through them. Small ponds and swamps, however, are present in practically all of them and these are especially numerous in the lowlands of south Georgia, where a few of these cases developed. The climate of south Georgia may be termed subtropical, that of the other sections visited temperate and never extreme.

CONSIDERATION OF CASES.

Distribution.—The 323 cases of pellagra which form the basis of this article are distributed among the three States as follows:[1]

[1]These numbers are approximately in proportion to the lengths of time spent in each State, and should not be taken as indicating comparative prevalence. In addition to this number there were reported to me by physicians in these counties 672 nonfatal and 431 fatal cases which make a total for the 25 counties of 1,426 cases. All of these cases were considered in my official report to the Surgeon-General. (Public Health Reports, March 7 and 14, 1913.)

Kentucky (three counties)	38 cases
South Carolina (seven counties)	161 cases
Georgia (fifteen counties)	124 cases
Total	323 cases

Race and Sex.—With reference to these points the cases are as follows:

	No.	Percentage.
White females	209	64.7
White males	91	28.2
Colored females	14	4.3
Colored males	9	2.8
Total	323	100.0

In the Kentucky counties which were visited negroes are in the minority, but in the South Carolina and Georgia counties they form a much larger proportion of the population and in places equal if not outnumber the whites.

Age.—According to age the 323 cases are grouped as follows:

Age.	No. Cases.	Age.	No. Cases.
0 to 5 years	15	45 to 50 years	23
5 to 10 years	23	50 to 55 years	21
10 to 15 years	11	55 to 60 years	20
15 to 20 years	12	60 to 65 years	11
20 to 25 years	42	65 to 70 years	8
25 to 30 years	34	70 to 75 years	4
30 to 35 years	37	75 to 80 years	1
35 to 40 years	38	Above 80 years	0
40 to 45 years	23		
			323

Marital Condition.—The marital condition of these pellagrins is as follows:

Single	83,	males 43,	females 40
Married	208,	males 50,	females 158
Widowed	32,	males 7,	females 25

Date of Onset.—On account of the vague nature of the early symptoms of the disease it was impossible to determine the exact date of the onset of the first attack in all of them. The year of onset, however, was determined in 317 of the 323 cases, but the month of onset was determined with a fair degree of accuracy only in 181 of them. The dates as determined with reference to the years and months are given below with the number of cases having their onset in each.

Year of Onset.	No. Cases Seen in 1911.	No. Cases Seen in 1912.
1912	0	53
1911	65	86
1910	30	29
1909	7	21
1908	8	5
1907	3	2
1906	2	1
1905	3	0
1902	1	0
1900	0	1
Not determined	2	4
Total	121	202

The month of onset of the 181 cases is shown in the following table:

Month of Onset.	No. Cases.	Month of Onset.	No. Cases.
January	2	July	25
February	11	August	14
March	18	September	4
April	27	October	5
May	37	November	2
June	36	December	0
			181

Occupation.—There is given below a list of the occupations which constituted the source of income of the families furnishing this series of cases, along with the number of cases in each group:

Occupation.	Total No. Cases.	Men.	Women.	Children under 15.
Factory	148	31	97	20
Mining	26	5	15	6
Agriculture	48	12	29	7
Trade	23	11	6	6
Clerical	18	8	5	5
Railroad Employment	5	2	1	2
Professional Work	5	2	2	1
Miscellaneous (laboring)	45	6	36	3
Without Occupation	5	5	0	0
Total	323			

Environment and Living Conditions.—Examination of the list of occupations given above will furnish some idea of the general

status of the people among whom the cases of pellagra in this series developed. The factory people were mostly of the cotton mill class, a class quite common in South Carolina and Georgia. These people live in little villages located around the cotton mills in which they work. Very few of them own their own homes or seem to care to, but live in cottages owned by the milling companies. They are nomadic in character and move from village to village as the notion strikes them. As a class they appeared to be poor, overworked and underfed, and to be living on what they earned from day to day or week to week. Although in many instances the total earnings of the working members of the families appeared quite sufficient for comfortable living, they did not seem to understand the art of applying this income towards the betterment of their living conditions. Many of the women and girls of this class work in the cotton mills and contribute to the support of their families. Early marriages and large families are the rule among them. In the counties of South Carolina and Georgia which I visited pellagra was found to be much more prevalent among the people of this class than among those of any other. In some of the villages visited the pellagra situation was alarming.

The pellagrins among the mining class were for the most part members of families of coal miners. They were living in small houses and shacks owned by the mining companies and located on the hillsides near the coal mines. They were found to be living a hand-to-mouth existence, depending for their support on the daily wages of the workers in the mines. The majority of them were living amid squalid surroundings, and many of them lacked even the rudiments of an ordinary school education.

The forty-eight pellagrins of the agricultural class were mostly of families of "renters" or "croppers." Some were landowners, a few of whom appeared prosperous. Many, however, were typical "Georgia crackers." The majority of the pellagrins in the remaining groups, while living in towns and in an environment somewhat better than that found in the mill villages and mining camps, still were living under conditions far below the average. A few, however, were enjoying the comforts of an environment which was far above the average.

Economic Condition.—An estimate of the economic condition was made in each instance. The results of these estimates are shown below:

Economic Condition.	No. Cases.
Poverty	258
Comfort	59
Affluence	6
Total	323

CONSIDERATION OF HOMES.

Location.—A classification of the homes is given here with reference to location:

A. With Reference to Population (at time of onset).	No. Cases.
In a cotton mill village	142
In a coal mining camp	24
In a town or suburbs	92
In the country	58
In a city	7
Total	323

B. Distance from Watercourses (at time of my visit).	No. Cases.
0 to 50 yards	31
50 to 100 yards	35
100 to 200 yards	49
200 to 500 yards	118
500 yards to 1 mile	51
1 to 3 miles	10
Distance not determined	29
Total	323

Sanitation.—The sanitary condition of the homes of the pellagrins in this series has been classified as follows:

Sanitary Condition.	No. Cases.
Good	11
Fair	36
Bad	249
Not visited	27
Total	323

GENERAL CONSIDERATIONS.

Insects.—From the standpoint of entomology the great majority of the pellagrous homes visited in this work would, without doubt,

have furnished interesting material for study. The ordinary bedbug was found to be present in some of the homes, was acknowledged to be present in others, and in very few indeed were conditions such as to lead one to suspect the absence of this and of other ectoparasites of man. It was the exception to find a pellagrin living in a screened house, although mosquitoes were said to be present in all of the districts visited. Malarial fever was reported to be common in some of the districts, but in others it was said to be practically unknown. Ordinary houseflies were present in practically all of the homes visited and were especially numerous in many of those where a pellagrin was confined to bed. The fly *Simulium* was found to be breeding in a number of the districts, but was not looked for in all of them. Two granaries, from which corn had been taken for families in which pellagra had developed, were inspected and were found to be heavily infested with weevils and moths.

Water Supply.—The source of the drinking water at the time of the onset of the disease in these cases was determined and is as follows:

Source.	No. Cases.
Wells: Bored	50
Dug	109
City or town supply	62
Well and city supply	12
Cisterns (stored rain water)	6
Surface water (wells, creeks, springs)	66
Varied	18
Total	323

Food.—It was learned that the great majority of the pellagrins in this series had been subsisting almost exclusively on food bought at the stores. The families among the cotton mill and coal mining classes were practically entirely dependent for their supplies on the small stores in the villages and camps, and despite the rural location of the homes of the pellagrins of the agricultural class they too were found to depend to a considerable extent for their food on the country grocery store. It was the exception to find a pellagrin who could state that even the major part of the food used in the family had been home grown. Necessarily the lines and quality of the groceries sold at these stores are regulated largely by the

finances, the tastes and demands of the patrons, and judging on this basis it can be said that the quality of goods sold at most of these stores was certainly not of the best, nor were these goods of the freshest. A list of articles of food having the largest sale at a store patronized by a number of people in whom pellagra had developed was made up for me by the storekeeper. This list, although presenting considerable variety, showed that much of the food used had undergone some process for its preservation, such as dessication, canning, etc. It seemed to be the consensus of opinion of the doctors practicing among these people that most of them were not receiving the proper quality and quantity of food, and that even when obtained in sufficient quantity it received hasty and incomplete culinary preparation. No constant difference, however, was found to have existed between the diets of the pellagrous and non-pellagrous members of the families.

Indian Corn.—Each one of the pellagrins considered here gave a history of the more or less regular use of corn products as articles of diet. Some acknowledged only a limited use of them, while others stated that they had "lived on corn bread and hominy." Hominy and meal seemed to be the forms of corn in most common use, and in all except three instances some of the meal used by the pellagrins previous to the onset of the disease had been obtaind at the stores, and in most instances all of that used had been so obtained. The stores were found to handle both locally grown corn and corn and meal imported from other States. The local mills of the districts visited were also found to grind both kinds, so it was practically impossible to determine the relative amounts of each which were being used by the people. In considering the subject of corn in its possible relation to pellagra in the districts visited, it must be remembered that these districts belong to the great corn-eating section of the country, where for many years corn, in one form or another, has been one of the main articles of diet for all classes, and where for many years the demand for corn has not been equaled by the local supply. This situation implies importation, which often requires considerable time for transportation, storage, and handling.

Relationship Between Cases.—Some of the gross relationships of the cases were determined by asking the pellagrins questions bearing on this point. These have been classified and appear below:

	No.
1. Case relationship in the families (same houses).	
A. Families having 1 case	264
B. Families having 2 cases	23
C. Families having 3 cases	6
D. Families having 4 cases	2
E. Families having 5 cases	1
2. Propinquity and contact relationships (miscellaneous).	
A. No known relationship to another case of Pellagra	91
B. Previous to onset had temporary association (as visit) with another case of Pellagra	24
C. Onset while living in the immediate vicinity of a Pellagrin	148
[1]D. Onset while living in the same house with a Pellagrin	50
E. Onset while living in a house previously occupied by a Pellagrin of another family	10
3. Relationships in food supply (stores).	
A. Stores among whose patrons 1 case of Pellagra developed	43
B. Stores among whose patrons 2 cases of Pellagra developed	13
C. Stores among whose patrons 3 cases of Pellagra developed	6
D. Stores among whose patrons 4 cases of Pellagra developed	4
E. Stores among whose patrons 5 cases of Pellagra developed	4
F. Stores among whose patrons 7 cases of Pellagra developed	2
G. Stores among whose patrons 10 cases of Pellagra developed	1
H. Stores among whose patrons 13 cases of Pellagra developed	1
I. Stores among whose patrons 19 cases of Pellagra developed	1
Total number of stores	75

These seventy-five stores were located in nine of the districts which I visited and in which pellagra was especially prevalent. It is believed that a complete canvass of the patrons of these stores, had it been possible to make it, would have brought to light more cases of pellagra than were actually seen. In these nine districts, as well as in others, the doctors reported to me many cases of well-developed pellagra which I was unable to see, and besides in these districts there were quite often seen persons who presented symptoms which greatly simulated those of pellagra, but to a degree not sufficient for a positive diagnosis. The presence of these borderline cases seems to me to be of considerable importance in considering the pellagra situation in a family or in a community.

Heredity.—None of my observations in this work has led me to believe that pellagra is hereditary. Of 58 children whose mothers

[1]Includes B, C, D, and E in Group 1 above.

had developed pellagra within one year after the birth of the child, 9 were dead (cause undetermined), but none was pellagrous; of 18 children whose mothers had developed pellagra within one year before the birth of the child, 2 were dead, but none of the living was pellagrous. Of 30 infants, who were being nursed by pellagrous mothers, none was pellagrous at the time of my visit, 6 were not well, and 24 were healthy.

Predisposing Conditions.—Of the diseases which were reported to me by the pellagrins and their physicians as belonging to their prepellagrous history and which seemed to have favored the onset of the disease may be mentioned the following: typhoid fever, septicemia, pneumonia, asthma, whooping cough, pulmonary tuberculosis, renal tuberculosis, malarial fever, syphilis, hookworm disease, smallpox, measles, alcoholism, morphine habit, lead-poisoning, diseases of the digestive system, as "indigestion," chronic constipation and others which might easily have been some of the early symptoms of pellagra, fistula, diseases of the gall-bladder, Bright's disease, anemia, muscular atrophy, poliomyelitis, paralysis, epilepsy, migraine, neurasthenia, arthritis deformans, "rheumatism," idiocy, imbecility; those referable to the sexual organs and reproductive functions in the female, as puerperal fever, eclampsia, salpingitis, lacerations of the perineum, menstrual disturbances, pregnancy and lactation. Operations and injuries seemed to figure to no small extent. Mental states, such as grief and worry, seemed to have paved the way for the development of pellagra in a number of instances. In not a few instances, however, it was not possible for me to determine, at least in the limited time at my disposal, just what might have acted as a predisposing cause.

The fact that 258 of the 323 of these pellagrins developed the disease under conditions of poverty cannot be without significance. The conditions of living, found in the great majority of these instances, including lax domestic and personal hygiene, and especially the questionable character of their food, seemed to have favored in some way the development of pellagra. I am inclined to think that the food used by these people contained elements which acted as a contributing cause of the pellagra among them, and probably also as the exciting cause, or as an aid to the exciting cause.

SUMMARY.

From the facts in the foregoing article summaries may be made with reference to the following points:

Race.—More cases developed among the whites than among the negroes.

Sex.—More cases occurred among the females of both races than among the males.

Age.—More cases developed at ages between 20 and 40 years than at other ages.

Marital Condition.—Among the married and widowed pellagrins the females predominate; the single pellagrins are equally divided between the sexes.

Dates of Onset.—More cases had their onset during the months of May and June than in other months, and more in 1911 than in any previous year.

Environment.—More cases developed under conditions of poverty than of comfort, and more under conditions of comfort than of affluence.

Relationship of Cases.—More cases developed in the vicinity of other cases than otherwise.

Heredity.—None of the facts seem to indicate that pellagra is hereditary.

Food.—The food used by the people in whom pellagra is prevalent deserves consideration as a possible etiologic factor.

ONE OF THE POSSIBLE FACTORS IN THE CAUSATION OF PELLAGRA.

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Of the various phases of the problem presented by pellagra, of its symptomatology alone can we be said to have even moderately full knowledge. Its epidemiological features and geographical distribution are as yet but imperfectly known, while in spite of the labors of many investigators whose researches have been directed toward the discovery of its etiology, the knowledge thus far gained leaves that important factor still largely within the realm of theory.

Many hypotheses of causation, based upon certain aspects of the disease or its environment, have been advanced, but none of these, perhaps, quite accounts for all the phenomena involved.

It is not the purpose of the writers to discuss these theories in detail nor to attempt to show the truth of any one of them, far less to propound a new, but rather to point to facts which may have a bearing upon the question.

If it be admitted that pellagra is a distinct morbid entity and not a mere symptom-complex, it is evident that the essential factors in its causation and spread must be uniformly active wherever the disease is endemic. In spite of this self-evident fact, the phenomena of the disease present many puzzling and apparently contradictory facts, under the varying conditions of environment and habit of its victims. Yet somewhere among these confusing phenomena must lie the constant element which is the cause of the manifestations of pellagra.

That the disease is due to an infection, is an opinion held by a considerable body of investigators and the arguments in favor of this hypothesis seem to warrant its serious consideration. Upon this hypothesis and the epidemiological features are based the theory that pellagra is an insect-borne disease. This theory, first formulated by Sambon, has been given prominence during recent years and has received the concurrence of able students of the disease.

If the disease is due to an insect-borne infection, a consideration of some entomological facts which appear to have significance in this connection, may be worth while.

As pointed out by Knab,[1] for an insect to be a potential transmitter of human disease, it is necessary that four factors should be active. These factors are the habit of biting man regularly, a more or less close association with him, a certain degree of longevity and finally, abundance. These biological characteristics assure the opportunity to bite man, the practical certainty that numerous individuals will bite him, not once only, but will secure successive blood meals and that a considerable number will survive beyond the developmental period of the hypothetical organism involved and again inflict bites.

The qualifications mentioned may vary in their relation to each other, as when great abundance and the persistence of the parasite in the blood of the vertebrate host, compensate for a less close association with man, which occurs among the mosquito transmitters of malaria.

Apparent exceptions occur in some of the Acarina or ticks, which are not usually domestic in any sense, yet convey certain diseases of man. But the power of this group to transmit the germs of disease through their progeny, together with their longevity and the duration of the life cycle, extend the possible period of infectivity to at least several years, in the case of some species.

The phenomena of pellagrous incidence as exhibited in America, differ in some important respects from those seen in some parts of Europe, according to authoritative reports.

Sex incidence in the Western Hemisphere shows a marked preponderance of female cases.[2] In some localities these bear a relation to those of males, apparently of more than three of the former to one of the latter, but always in marked preponderance. This seems not to be the case in Europe, where the cases among females, although somewhat more numerous than those of males, are in much smaller majority than in America.[3] There may be several reasons for this difference in the proportion of the two classes of cases in these countries, but the most obvious is that of habit and occupation. The peasant woman of Europe shares the work of the men of her family in much greater degree than is the case among the women of any class in this country. Whether at

work in the fields or about her home, the peasant woman is exposed in much more nearly equal degree to the same conditions and liability to infection, whatever be its source. How this may influence the occurrence of the disease in the two sexes will be referred to later.

According to publishd statements, the class of the population affected with pellagra is much more sharply defined in Europe than in America. If we may believe these statements, the disease is confined almost exclusively to the strictly rural population and to those in the most abject circumstances in life. Its occurrence among the well-to-do is the exception.[4] In the United States, no such sharp line can be drawn and no class of the community is free from its attack. That city and town dwellers are exempt is an assertion so frequently made as to have become practically axiomatic. If true of the towns and villages of Italy, as asserted by Sambon,[5] it is not applicable to urban communities in America, except possibly, those of the largest size, although it is undeniable that those whose occupation or residence is in an essentially or truly rural environment are more subject to the disease. But as we shall show, very many American towns of a size deserving the designation of cities, are from the view point of possible insect transmission, essentially rural communities.

Assuming the possibility that pellagra is an insect-borne disease, whose causative organism is present in the peripheral circulation, a review of the biting insects which might be involved in its transmission, centers the attention upon the body parasites, fleas, lice and bedbugs and the winged suctorial insects, such as mosquitoes, stable flies and the members of the genus Simulium or buffalo gnats.

Beall[6] has pointed out that the infection of pellagra seems to be incurred "in the home, or around the home," basing his conclusion upon two facts: the marked preponderance of female over male cases and that of males affected, a large percentage are of the age at which the time spent in the home is greatest. He believes that the preponderance of female over male cases is due to the greater exposure to infection and not to greater susceptibility or lower resistance, which is, as he says, contrary to medical experience. The higher rate of infection in very young and elderly or old males, he says, is also due to greater exposure.

In this connection, it is noteworthy that in malaria, an insect-borne, protozoal disease, there is no difference in the susceptibility of the sexes to the disease.[7] Observations by others appear to bear out his conclusions and from this standpoint, a consideration of the classes of insects mentioned above, brings out certain facts.

The mosquitoes of the principal regions in which pellagra is endemic, are either crepuscular or nocturnal in their biting habits and men, in their hours of leisure or during sleep, would be exposed to mosquito-borne infection equally with women. There are also facts of distribution in connection with this group which seem to exclude them from grave suspicion of pellagra transmission: As an instance, the distribution and abundance of mosquitoes in certain parts of the Southeastern States is in inverse ratio to the occurrence of the disease.

With the exception of the facts of distribution, those just cited as probably excluding the night-biting mosquitoes as potential carriers of pellagra, apply with equal force to the bedbug. The spread of the disease, the occurrence of isolated sporadic cases, the by no means rare infection of persons whose habits and condition in life go far to protect them from attack and the large number of families in which but one or two members are affected in spite of habits conducive to indiscriminate attacks, seem to argue against the bed-bug as a possible carrier. The long life of these insects and their resistance to starvation, with their persistence in infesting a building when once they have gained lodgment are undeniable. These habits might be regarded as indicating them as the source of the so-called "place infection" of pellagra. This phenomenon has, however, by no means been shown actually to exist, and it is doubtful if the habits just mentioned outweigh those which seem opposed to its incrimination.

The head and body lice must be considered, especially in view of the comparative abundance of the former species in some localities where pellagra is prevalent, but here, too, it is difficult to reconcile the habits of the parasites with the sex incidence of the disease, while in view of the frequence of its occurrence in individuals of unimpeachable personal habits and associations the agency of these insects is inconceivable. The epidemiological facts regarding the incidence and spread of pellagra, strongly suggest a winged carrier.

rather than one dependent upon the movements of its host for the means of migration.

Fleas are usually considered among the most ubiquitous of insects, yet it is rarely that the dwelling of a country home is more heavily infested by these insects than the barns and other outbuildings with their animal tenants. Yet if this is not the case, how can the infection of the female members of the household in greater proportion than the males be accounted for if the flea is to be incriminated? It is difficult to see how, under the circumstances, women could be more exposed to attack than men.

Under such conditions as exist in the mill villages of South Carolina, the family dog or cat which is not infrequently kept, might be blamed and the infection "in or around the house" explained. But the histories of many cases taken in these villages show a rather small number of instances in which reports of the attacks of fleas can be obtained.

Furthermore, it must be borne in mind that most fleas are highly selective in their choice of host. The individuals of the species which normally attack domestic animals, in this locality the most common being the cat, dog and chicken fleas, when from expedience they resort to man, usually remain upon him but a short time and frequently leave him without inflicting bites. The transferrence from man to man of such fleas, probably happens but seldom under ordinary circumstances. We have been unable to obtain the human flea, *Pulex irritans*, in South Carolina, and although probably to be found in the State, it can scarcely be a serious pest.

It is claimed that endemic pellagra always occurs in close proximity to the haunts of *Simuliidae* and that, therefore, these insects are the transmitters of the disease.

In the regions in which pellagra in endemic, the genus *Simulium* is represented by many species, none of which has a range as wide as the distribution of the disease. The biting habits of these species with regard to man are very imperfectly known, but from recorded observations, it appears that of the American species, some attack man readily, while others seem never to do so. Some bite him with great infrequency, while still others will bite in one locality but not in another.[8]

The great abundance of *Simulium*-infested streams in many localities in which pellagra is prevalent is unquestionably highly sug-

gestive, but until the identity of the species present and the biting habits of those species *in that locality* are determined, the significance of the condition is greatly lessened. While knowledge of the biting habits of the group remains in its present incomplete state, the proximity of a *Simulium*-breeding stream to the point of origin of a case of pellagra does not warrnnt a definite conclusion of attacks by the adult flies or their connection with the infection.

There are pellagra infested localities in South Carolina, the numerous streams of which contain Simuliuin larvæ in numbers sufficient to justify the belief that if the adult flies were in the habit of attacking man with regularity, some impression would be made upon the memories of residents of the neighborhood. Yet in these localities systematic and diligently pursued inquiries have failed to elicit more than an occasional report of the attacks or noticeable presence of such flies, even when dwellings have stood within a few feet of *Simulium*-infected water. In places infested by mosquitoes, to even a moderate degree, their presence is always well known, as is likewise the case in localities where sand-flies, (*Phlebotamus* and *Ceratopogon*) are found. With due regard for the general unreliability of popular observations and reports upon such matters, it is inconceivable to the writers that flies of the appearance and habits of the Simuliidæ could be present and attack man in sufficient numbers to account for the prevalence of the disease, yet fail to attract attention and to remain in the memories of their victims.

It is said upon good authority that the Simuliidæ are short lived, as the short duration of individual outbreaks seems to indicate. This would lessen the probability of the transmission of the virus of pellagra through their agency, unless, as is very possible, the developmental period within the insect is of short duration. Should this be the case, the short life of the insect would reduce the chance of a second human being receiving an attack after the infection of the fly.

None of the species of *Simulium* is closely associated with man. As has been pointed out, with certain exceptions, all of the insects known to be carriers of human disease are more or less closely associated with him, the transmission in the case of the exceptions being effected by factors which do not exist in connection with the flies under consideration. Less close association is always com-

pensated for by great abundance, and persistent attack, two attributes which can not be said to be generally manifested by *Simulium* species in South Carolina:

Representatives of the genus appear to be totally absent from some arid and semi-arid regions in which pellagra is known to occur.[9] If it can be definitely shown that cases occurring in these arid regions originated there, that fact would in itself eliminate *Simulium* from consideration in connection with the disease. It is known to us that pellagra is endemic in a locality of large area in which, *Simulium,* though present, occur in such exceedingly small numbers as to strongly indicate that transmission by them would be impossible.[10]

Large towns are not frequented by these flies, although it should be pointed out that *Simulium* larvæ have been taken by us in small streams in South Carolina within the built-up sections of towns of several thousand inhabitants. At the same time, no satisfactory reports of the attacks of the adult flies could be obtained.

Conforming much better to the requirements pointed out, is another blood-sucking insect, *Stomoxys calcitrans,* the biting stable fly. It is of cosmopolitan distribution and has practically uniform habits throughout its range. In most places it is abundant, even excessively numerous, and is closely associated with man and his domestic animals, breeding about his outbuildings, frequenting the vicinity of his dwellings and even entering them, sometimes in considerable numbers. Although it prefers to attack domestic animals, it readily bites man and with frequency, but some slight irregularity, depending, apparently, upon meteorological conditions and the immediate availability of its normal prey.

How long the stable fly lives is not known with certainty. Its length of life is probably considerable and it breeds throughout the summer season, appearing in early spring and persisting until late fall. In these characteristics of association with man, blood-sucking habits and a reasonable degree of longevity, it conforms to our ideas of the potential disease-carrier, and if connected with the transmission of pellagra, it may explain certain epidemiological phenomena of the disease.

As we have before stated, the majority of the cities and towns of this region are, from the standpoint of *Stomoxys* propagation and distribution, rural communities in that they offer facilities for

both of these functions, which are not inferior to those existing in country districts. The densely built-up business sections are of small area when compared with the spaciously planned residential districts in which houses are surrounded by lawns and grounds of greater or less extent and the keeping of domestic animals, principally horses and cows, is almost universal. Breeding of these flies takes place, not only about the private stables referred to, but in and about the public stables and wagon yards in the business sections. As a result, the stable fly is to be found in all parts of such towns and in the smaller ones are very numerous everywhere.

In such towns in this region, pellagra occurs endemically.

The common habit of *Stomoxys,* of frequenting and entering dwellings under prevalent conditions, would explain, were the fly incriminated, the high percentage of cases among those, most of whose time is spent at home. In the mill villages of South Carolina, where many cows are kept, they are, in the majority of cases, milked by the women of the family, as is usually the practice upon the small farms also. Very many reports are received of the attacks of these flies upon the milkers and a large percentage of persons interviewed in these places gave accounts of having been bitten.

The number of individuals of this species, not infrequently found in the living rooms of houses of a certain class, would go far to explain the occurrence of several cases in a single family, as the close association would favor the communication of the disease. This probability is heightened by the fact that Stomoxys does not usually take a full meal at one time, as do mosquitoes, but passes from one man or animal to another.[11]

Domestic animals are frequently followed for long distances by these flies and they are readily transported by railroad cars and steamships, as we have ourselves observed. It can be readily seen that droves of cattle, or under modern conditions, cars in which live stock is being carried, might offer to infected flies means of migration to distant places and cause isolated infections, thus accounting for sporadic cases whose histories show no apparent exposure to the disease.

In conclusion: If pellagra is caused by an infection, especially if of protozoal origin, and is transmitted by an insect, the present state of our knowledge leads us to the provisional belief that the following deductions may be tenable.

Under conditions existing in the region of pellagrous endemicity in South Carolina, the lice, fleas, mosquitoes and bedbugs show characteristics of habit, distribution or abundance which appear to exclude them from serious consideration in this connection.

The biting habits and, to a certain extent, those of distribution of the flies of the genus *Simulium*, together with their lack of habits which brings them into close association with man, seem to present weighty arguments against the incrimination of these gnats as the active agent in the transmission of pellagra.

The cosmopolitan biting stable fly, *Stomoxys calcitrans,* from its distributional and biting habits, its close association with man, its conformation to the obvious requirements of the disease-transmitting insect and the agreement of its special characteristics with the phenomena incident to the occurrence of pellagra, offers strong reasons for its consideration under the premises.

It is hoped that attention may be directed to this fly and observations bearing upon its possible relation to the disease be generally made.

We would add that should a causative organism be shown to exist, which is a bacterium rather than a protozoon, and should this organism invade the body through either the mouth or the skin, the house or typhoid fly, *Musca domestica* and the flies whose habits at all resemble it, would lie under strong suspicion. It is needless to say that the house fly is excessively abundant and of universal distribution in the region studied.

We are also aware that the communication of pellagra in a purely mechanical manner by biting insects is a possibility and if shown to exist, would radically change our ideas as to the insects which may be involved.

Finally, we wish to repeat that essential uniformity of causation must be assumed to universally exist and that the demonstrated failure of a supposed etiological factor to account for the phenomena of pellagra in one locality must serve to exclude it from consideration as a factor in another.

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[8]A revision of the American Simuliidae, north of the southern boundary of Mexico, which is now being made, indicates in certain instances, that what have heretofore been regarded as single species are in reality composed of several distinct forms. It is highly probable that the apparently contradictory reports of the biting habits of certain species actually refer to two or more forms and if this is shown to be the case, it will serve to clear up one important point in the biologies of the American species of the group. Such a conclusion would tend to weaken the position which investigators have assigned to these flies in connection with disease transmission. There is every reason to believe that what is true of the American species is true of the European also, and that more exact study will show more numerous forms to exist there, each with special habits.

[9]Beall, K. H. Bull. Tex. State Board of Health, Vol. 5, No. 9, 1911.

[10]Endemic Pellagra occurs in Barbados, W. I., yet no species of Simulium has been found to inhabit that island in spite of the systematic work of government and other entomologists. The existence of any species whose habits conform to those uniformly prevalent in the known representatives of the genus, is practically precluded by the geological and topographical features of the island.

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PELLAGRA AND THE SAND-FLY.

By S. J. HUNTER, State Entomologist, University of Kansas, Lawrence, Kansas.

Since 1776 when the Patriotic Society of Milan offered a prize for the discovery of the cause, the Etiology of Pellagra has been a subject of serious inquiry. It is still a question whether it is toxico-chemical, toxico-infectious or due to a specific infection by moulds, bacteria or protozoa.

Three theories have been advanced as to the cause of this disease: (1) the zeistic theory based on the work of Ballardini, in 1845, giving corn poison due to the excessive use of corn products as the cause, supplanting the old theory of faulty metabolism; (2) the cotton seed products poison theory of Mizell, in 1911; and (3) the sand-fly theory of Sambon, dating from 1910. The first two rest on malnutrition, the last on the action of a parasite.

Since this paper deals with the parasitic theory, the grounds on which Sambon bases his theory may properly be outlined here:

A. The endemic center of pellagra in Italy have remained the same since the disease was first described.

B. The season of the recurrence of pellagra coincides with the season of the appearance of the full-fledged sand-fly, even to the extent that if the spring is early or late, the sand-fly is early or late in appearing, and pellagra cases are correspondingly early or late in their appearance.

C. In centers of pellagra infection whole families are attacked at times simultaneously.

D. In non-pellagrous districts the disease never spreads to others with the advent of a pellagrin from a pellagrous district.

E. In the case of a family which has removed from a pellagrous to a non-pellagrous district, the children born in the former district are pellagrins, while the children born subsequent to removal to a non-pellagrous district do not develope the disease.

F. The disease is not hereditary, although infants a few months old may become infected, especially if taken to the fields in pellagrous districts, where their mothers work during the season when sand-flies are in evidence.

G. Pellagra is not contagious, but is transmitted to each individual by an infected sand-fly.[1]

In Kansas the latter part of July, 1911, the first authentic cases, those of a mother and child, were diagnosed by Dr. E. E. Liggett, of Oswego, the attending physican. Dean Crumbine, of the medical school of the University of Kansas and Secretary of the State Board of Health, expressed an earnest desire to have the presence of the sand-fly ascertained for that locality. Accordingly I began, on August 1, a survey of the region. The streams were high and muddy from recent rains so that adults were first sought. An extended opportunity which I enjoyed for study of this insect some years ago in the Mississippi Valley, between Keokuk and Fort Madison, Iowa, rendered familiar the workings of the adult females on horses, especially young colts, on which, after warm rains, the attacks were so numerous and severe as to denude the animals' ears and throats, exposing patches of raw flesh.

Accordingly, the first day at Oswego, specimens were taken from the ear of a brood mare. Later, when the local streams had fallen, abundant larvæ and pupæ were found. A small stream which passed within 400 yards of the home of the pellagrins had a large colony attached to the tree roots forming riffles in the water. About a mile farther down the same stream a series of rock riffles were well covered with larvæ and pupæ. Here seemed to be an excellent opportunity for a serious endeavor to apply the Sambon theory.[2]

The lines of investigation which I determined to follow were: transfusions on guinea pigs and monkeys and transference of flies, exposed to the pellagrins, to monkeys and guinea pigs. In the experiments with each exposed animal there was a check or unexposed animal.

The transfusions and inoculations gave no positive results. Temperatures of the guinea pigs and monkeys were taken twice a day without any appreciable change. As this subject has been covered in a paper by Anderson and Goldberger,[3] we will pass to what we consider the more important phase of the Sambon theory, viz.: the role of the sand-fly.

His theory is protozoal and from analogy with the etiology of malaria, the parasite of pellagra in all probability would have to pass one stage in the body of its intermediate sand-fly host before

it could resume its life in the human body. This hypothesis being true, transfusions obviously would be without results.

Taking up the sand-fly, then, the only species found in Kansas thus far is *Simulium vittatum* as determined by Johannsen. *S. reptans* is the species referred to by Sambon and reported on this continent from Greenland only. Since several species of the genus Anopheles transmit malaria, it would seem permissible to consider other species belonging to the genus Simulium than that of *S. reptans,* referred to by Sambon. *S. vittatum* is distributed in Kansas, as far as our survey has proceeded, along Turkey Creek, a tributary of the Kaw in Wyandotte county, along the Marais-des-Cygnes in Franklin county, along the Neosho and its tributaries in Allen and Labette counties, along the Arkansas in Sedgwick county, along the Walnut in Ness and Rush counties, along Big Creek and other tributaries of the Smoky Hill in Trego and Ellis counties, along the tributaries of the Saline River in Russell county, and along the small streams in Jackson and Douglas counties. A careful survey of the southwestern part of the State has thus far revealed no breeding places or adult forms of this insect. The most western point then is in Ness county. The survey is not yet complete, but will be continued until the entire State has been covered.

For the location of the pellagrins we have Allen, Chautauqua, Montgomery, Labette, Shawnee and Meade counties. All cases are in the midst of the sand-fly territory, except the Meade county case, and this man, a resident of that region for twenty years, spent the year of 1910 in the South. The Allen and Labette county cases are endemic. None of these patients have ever been out of the State, so it would seem that the cause now exists in the State.

For our experimental work the Oswego pellagrin, a woman aged about 35, now in the second season of the disease, was used, and she very willingly did her part.

In this study some interesting observations were made on the life history, methods of oviposition, character and number of eggs deposited by each female. In all, 1,282 live sand-flies were used and this phase of the work extended from August 21 to November 4. The plan was to divide the number of flies intended for each experiment into two lots, the one lot to be exposed to the pellagrin and then to the subject of experimentation, and the other exposed to the check.

Ten guinea pigs and two monkeys were used and the temperatures of all were taken morning and evening daily. The number of live flies exposed to the pellagrin and then to the guinea pigs was 499, the number of live flies exposed to the pellagrins and then to the monkeys was 197. A part of those exposed to the pellagrin were reserved for fixation and sectional microscopic examination in the laboratory. Since only the females bite, the relative number of the sexes is important. In a count of 488 specimens, 219 or 42 per cent. were females.

Earlier in the season the flies did not seem to bite the patient, but beginning with October 12 they attacked her, biting freely, drawing the blood perceptibly from the pellagrin's arms. These flies were then divided, part placed in the fly-proof cage with the male monkey; part with the guinea pigs. Repetitions of the same experiment were made almost daily during the stated period.

November 7 the male monkey began to be less active. On the morning of November 8 he appeared decidedly ill, crouched on the floor of the cage and was both unwilling and unable to ascend to his perch. He remained ill all day, getting worse till late in the afternoon he became flaccid and motionless save for a high rate of respiration, ranging from 45 to 60 per minute. His temperature was 103.6 F., a little above normal. He appeared about the same the next morning, but improved a little during the day and continued the same until November 12, refusing all food, but drinking water freely. He was placed in charge of Dr. Boughton, pathologist, and Dr. Skoog, neurologist, of the university. He was chloroformed, autopsied and the brain and spinal cord were studied by the nerve specialist. This monkey was taken from the university hospital group. It now appears that some eighteen months ago this monkey was exposed to poliomyelitis. While the time is remote, nevertheless, the exposure obviously introduces a complication which will make it unsafe to depend on this instance, unless substantiated by many pure culture corroborations.

As far as our information goes this is the first recorded instance of an endeavor to apply the Sambon theory along these lines. The work of last summer served to establish a satisfactory technic and to furnish material for examination in the winter.

This season has been one of unusual precipitation and with it a noticeably less number of larvæ and pupæ in the streams of the

eastern part of the State, due, in all probability, to the inability of the female to find suitable places for oviposition. The female, when about to deposit her eggs, seems to select with a rather remarkable degree of precision a certain situation. This is a dry rock in a shallow riffle, from under which the water bubbles up. She rests upon the dry portion of the rock and deftly recurves the ovipositor so as to deposit the eggs at the very edge, kept moist by the bubbling water. I have heard of female sand-flies plunging beneath shallow water falls to oviposit on the rocks thereunder. Neither I nor my graduate student who is working with me, Mr. W. T. Emery, have observed this action.

There are three principal broods of the fly in Kansas, one April, then July, and the last in October. During the month of August, 1912, it was almost impossible to find a larval or pupal form in a running stream. At other seasons our survey goes to show that it might be possible to find immature stages in any swift running brooklet in the State. Whether this scarcity of flies this season is significant or not it may not be out of place to mention the coincident fact that there has only been one new case of pellagra reported for the year.

It has been said that the sand-fly will not bite human beings. On the contrary we found that the females of the October brood bit the pellagrin even when in captivity, and in our biological survey camp our men sleeping out on the cots in the open were frequently disturbed about daylight by the biting of these flies. The flies were captured in the act of biting and determined so that there could be no mistake about the species.

It seems probable that the females bite better after oviposition. When held in captivity they must be kept in a gauze sleeve or receptacle. When retained in bottles they seem to bruise their antennæ to such an extent as to render their sense of taste or smell useless.

The field presented in Kansas for the study of the etiology of pellagra has one factor which commends itself. That is, it is "virgin soil." As far as medical records go last season was the first period of the disease in Kansas and all of the subjects save one in Kansas were born and bred therein and have resided continuously within its borders.

The disease has appeared only among the inhabitants, with one exception in a western county, in the southeastern portion of the

State. Of the nine cases so far known it is interesting to note that five have spent a part or all of their lives in the town of Iola. Now this portion of the State being in the oil, gas and coal region contains the largest floating foreign population. The pellagrins on record are native Kansans.

Saggital and transverse sections have been made of flies which have bitten the pellagrin, and fixed with standard fixatives. In one specimen a very suggestive organ was found located outside of the stomach wall.

The best biting time for this season's work has not yet arrived.

We have a number of monkeys shipped direct from India last spring and now sufficiently acclimated to warrant, with proper care, a healthy existence for some time. There is every reason to believe, therefore, that a favorable opportunity is at hand for either negative or positive results with reference to the sand-fly as an agent in this problem.

Referring again to the Sambon theory we find in Kansas that the sand-fly and pellagra are coexistent; that for the two seasons the number of Pellagrins has borne a rough proportion to the number of sand-flies.

As yet there has been no definite evidence fixing the sand-fly either through study of its anatomy or through experiments with it as a factor of transmission, to connect it in any way with the disease.

[1]1. Since this paper was read innoculations were continued to close of season. The last dates were on December 16, 17, and 20, using flies that had emerged on the 12th and had bitten the pellagrin on the 14th.

Summing up the work of the past two years:

1. The number of sand-flies has been directly proportional to the number of cases of pellagra.

2. The first appearance of the cases of pellagra is coincident with the principal broods.

3. Just succeeding the time of the principal broods the flies appear to bite more vigorously.

4. Sand-flies which have fed on human blood live several days longer than those which have not been so nourished, thus favoring an incubation period for a parasite, if such there be.

5. Pellagra, thus far in Kansas, has appeared almost entirely in one restricted locality. Of the nine cases recorded last year five were traced back to one town. In this region the flies are widely distributed and unusually abundant.

As far as our history of this subject goes the appearance of pellagra in Kansas is a recent occurrence. Nearly all the cases are those of natives who have never been out of the State.

From this it would seem that the etiology of pellagra exists in Kansas.

The situation here is not complicated through long standing conditions. It is the purpose, therefore, to continue this phase of the work and with it the correlation of the clinical and pathological phases by the medical school of the University of Kansas.

[4]2. Dr. Harris has recently announced the production, experimentally, of pellagra in the monkey. According to his work the monkey is a susceptible animal. It should, therefore, respond to any virus which the sand-fly or other insect might introduce.

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[2]In the subsequent work we had the hearty co-operation of the attending physician, Dr. E. E. Liggett, and Dean Crumbine. I have also had the valuable assistance of W. T. Emery, one of my graduate students.

[3]Public Health Rep., 1911, XXVI., 1003-7, 1911, who obtained similar results.

[4]Journal American Medical Association, XL, No. 25, June 21, 1912, pp. 1948-1949.

SAMBON, THE MAN, AND HIS LATER INVESTIGATIONS OF PELLAGRA.

By J. H. TAYLOR, M. D., Columbia, S. C.

On several previous occasions at pellagra conferences and clinics here, we have presented before you Sambon's views upon the etiology of pellagra. By some they have been accepted, by others rejected. At this meeting also, we presume, his theory will have its advocates and opponents. It is hardly necessary for us to say that, in the absence of definite proof to the contrary, we still uphold the doctrine of a probable parasitic origin for pellagra. The details of American investigation into the subject we leave to the active workers in the field. For a few moments, however, we wish to invite your attention to Dr. Sambon, the man and scientific investigator, and to what he has written about his latest observations upon pellagra in southern Europe, subjects both new and, we trust, not without interest to you.

Now forty-one years old, Louis W. Sambon was born in Italy of a French father and an English mother. There he grew up in a charming atmosphere of culture, his father being an antiquarian of note and his brother a numismatist whose honor it was to instruct the Italian King in the science of medallions and coins. He himself, in his younger days, was an eager student of natural history, and while living at Naples, made a study of vulcanology, and wrote papers on Vesuvius, Monte Nuovo, Ætna and the Lapari Islands.

Graduating with honors in medicine from the University of Naples in 1891, he, a year later, became an assistant surgeon in the Italian army. Soon, however, on account of his splendid ability and linguistic attainments, he was sent to foreign countries on various governmental missions, and, later, returning to Rome, devoted himself to the study of the natural sciences, geography, history, and medical archæology. Owning himself a vast and important collection of medical antiquities, he has written exclusively on this subject, and we may mention especially in passing an article on the Ancient History of the Plague, wherein he shows conclusively that the Romans, Egyptians and other people of antiquity recognized the

definite and close relationship between this disease and rats, a relationship that we moderns have but just worked out.

In 1897 he went to England, where he soon attracted the attention of Sir Patrick Manson by an article on acclimatization,[2] and in an interview later Dr. Manson recognized in the young Italian the scholarly thinker whose splendid achievements have since more than verified his estimate of the man. He was later appointed to the chair of parasitology in the London School of Tropical Medicine, which was just then being organized by Dr. Manson as the first of its kind, and from that day his energies have been bent upon advancing our knowledge along these lines, emphasizing especially the relationship of parasites to the various tropical diseases.

Because of his intuitions and insights, Sambon is recognized as an investigator himself, but his theories and conceptions have also served to stimulate other less imaginative workers in the broad fields of medical science. As Dr. Cantlie has said, "Men of this type are rare. We have many observers, but few thinkers." In tropical medicine, with the possible exception of Sir Patrick Manson himself, no one man has stirred the pool so deeply.

It was Sambon who in 1897 enunciated the theory, recognized now as an established fact, that not the climate renders the tropics uninhabitable to the white man, but the tropical parasitic infections.

One of the most fascinating chapters in medical history deals with the experiments conducted in 1900, designed to prove beyond a doubt that malarial fever is produced through the bite of the infected anopheles, mosquito, and, further, that protection from the bite of this insect gives immunity. Dr. Sambon personally demonstrated the latter by several months' residence in a screened hut in the most unhealthy portion of the Roman Campagna.[3]

Surely we all know how, by a careful analysis of the distribution of the glossina palpallis, he designated from his study in London this fly as the transmitting agent of the trypanosome that Castellani had just discovered, and stated that this trypanosome must be the cause of sleeping sickness, and, furthermore, that the ability to infect is transmitted from parent fly to offspring, all now well established facts.

To our mind, one of his most striking prophetic suggestions deals with our own spotted fever of the Rocky Mountains. Before the publication of Rickett's Papers in 1910, Dr. Sambon took exception

to Stile's findings, and in an article written for Allbut's System of Medicine in 1907, favored the protozoal nature of the disease and its transmission by ticks. He suggested that the Rocky Mountain fever was but a local variety of typhus fever, and that the latter is not directly contagious, but transmitted by blood-sucking insects, such as the body louse and the bedbug. In 1910 Dr. Nicolle[6] at the Institute Pasteur proved by actual experiments that typhus fever is in very truth conveyed by the body louse, thus verifying a suggestion Sambon had made, based on a very careful study of the epidermology of the disease.

Another sidelight on the man's amazing scientific versatility is spoken of by Dr. Cantlie.[7] It appears that Dr. Andrew Balfour, of Khartoum, read a paper before the Section of Tropical Diseases at the British Medical Association in July, 1907, concerning the presence of a parasite he had found in the blood of Sudanese fowls. "Dr. Balfour, in common with Laveran, Nutall, Leishmann, Manson, Daniels and others to whom he had shown his specimens, considered the parasite to be a Babesia, but Dr. Sambon, in the discussion on Dr. Balfour's paper, stated that on examining a slide given to him by Dr. Balfour he had come to the conclusion that the parasite was not a Babesia, but the coiled-up endoglobular stage of a spirochæta, possibly S. gallinarum with the cromatin core broken up into a number of separate granules. Little notice was taken at the time of Dr. Sambon's remarks, but Dr. Balfour states in 1908 that on further investigation he is in accordance with Dr. Sambon's views. The discovery is of the utmost importance, as it shows definitely that the spirochæta are protozoa and not bacteria, and discloses an endo-corpuscular stage which had hitherto escaped observation."

We believe that in the foregoing there is sufficient proof of the man's almost unerring judgment, certainly sufficient to make us read with unconcealed impatience the occasional slighting references in American print to his suggestions regarding the probable protozeal nature of pellagra.

In concluding our remarks on Dr. Sambon's personality, we would say further that science owes to him the description of thirty-eight new parasites in man and in animals, and his vast knowledge and his true genius of intuition have enabled him to construct a new classification for the hemaprotozoa. Up to 1911 his published scientific articles and contributions numbered sixty-two.

This rough outline will, we trust, afford some of you, as it has us, a clearer conception of the somewhat evasive personality of Dr. Sambon. Most of our statements are based on an editorial in English by Dr. Cantlie, mentioned above, and on the contents of a sketch of Dr. Sambon appearing in an Italian medical pamphlet, "La Malattia Del Sonno"—Roma, 1908.

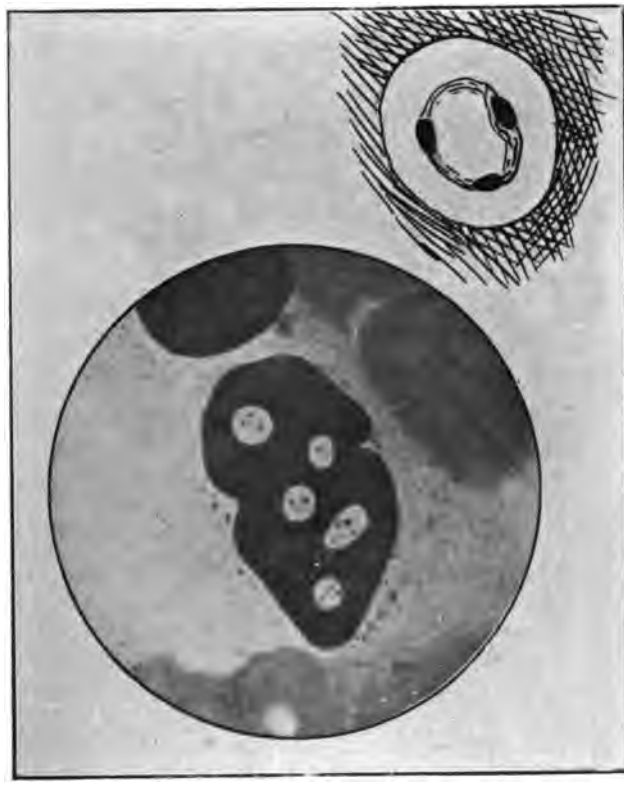
These articles, together with many of his scientific publications, were recently obtained from England, and had not this good fortune befallen us we should have known little of this man to whom science owes so much.

Now, regarding Dr. Sambon's recent investigations: He, in company with Dr. Chalmers, of the Ceylon Medical College, again in 1911 and during the past spring visited several pellagra districts in Roumania, Austria, Hungary, Italy, Spain and France, in an effort to further substantiate the results of his first expedition to Italy, in which you will recall he obtained many striking facts that seemed to show a relationship between pellagra and certain biting insects of the family simuliidæ.

Not the least interesting observation made by these men was the presence of a protozoal organism in the brain and spinal cord of a young female Roumanian pellagrin, who died in the acute stage of the disease the moment they entered the pellagrosario of Roman. Unfortunately, they have since had no further opportunity of making autopsies under favorable conditions, nor have they been able to pursue the matter owing to unfavorable meteorological conditions and imposed restrictions.

This new organism was examined and pronounced to be of protozoal nature by Sir Patrick Manson, Dr. William Leishman, Professor Minchin, Dr. Low and other well known parasitologists, both in England and on the continent. Other minute bodies, possibly related to this parasite, were found in the blood, in the cerebrospinal fluid and in the liquid from skin lesions of other pellagrins by Drs. Sambon and Chalmers, and independently by Dr Low. Of course, the exact relationship of this organism to pellagra, if there be any, is a matter that requires further investigation. Nevertheless, it is a most engaging observation, and will add greatly to the zest of further search.

Their epidemiological findings, furthermore, are of surpassing interest, and while the question remains still an open one, yet Dr.



Sambon's views have been materially strengthened. The results of their work we cannot do better than present to you in Dr. Sambon's own language, embodied in a personal letter to us, dated August 21, 1912.

Since the publication of my "Progress Report" on pellagra, my researches have been greatly hampered by all kinds of adverse conditions. Nevertheless, I have been able to visit the best known pellagra stations in Europe and collect much valuable information. I am now more than ever convinced that pellagra is an insect-borne protozoal disease.

Both last year and this spring, I have been accompanied in my travels by Dr. A. J. Chalmers, who has been a most convinced supporter of my theory. Indeed, a few months ago he went purposely to Egypt, at his own expense, to investigate pellagra in the Nile Delta.

In all countries visited by me (Italy, Spain, Austria, Hungary, Roumania, France), the true pellagra stations were found to be closely connected with more or less swiftly running streams, just as malaria is associated with stagnant waters, and everywhere, I found the disease associated with Simuliidæ, just as malaria is associated with Culicidæ.

I always examined children very carefully, and, contrary to the almost universal opinion, I found that, in the true endemic centers, children are invariably affected just as they are with malaria in malarious localities. Therefore, I do not consider a place to be a true endemic center of pellagra unless I find the disease in very young children who have never been out of the locality. The two youngest pellagrin children seen by me were three and four months old, respectively, when first attacked. Between six and eighteen months of age their number is legion.

I have often found pellagrins and, sometimes, many pellagrins, in places which certainly were not endemic centers of the disease. In such places the patients were adults. Infants and very young children were never affected, only occasionally a few of the older children. Pellagra affects almost exclusively field laborers, but only such as are stationed within its endemic areas. It is a disease of long duration, often exhibiting long periods of latency, and pellagrins soon become restless, and are therefore especially prone

to migration. All these facts must be taken into account when studying the topographical distribution of the disease.

When I left Italy, in 1910, I brought to London a young pellagrin girl (Muziata Bettachioli) from Citta di Castello, Perugia. During the spring of 1911, she did not present any skin eruption, but only a strange, unreasonable behavior, which made my wife somewhat anxious on account of the children, who often played with the little Italian peasant. This spring, whilst I was in Italy, my wife wired that Muziata had developed unmistakable pellagra. Her hands and face exhibited a slight erythema, which was followed by marked desquamation; she complained of vertigo and headache and behaved in the same peculiar manner as in the year previous. Now, this girl had lived with us in London and had neither tasted nor seen maize since she left Italy two years ago. She was in splendid health, and had become almost as fat as a pig.

Dr. Warnock, director of the Cairo Lunatic Asylum, told Dr. Chalmers that he had noticed the recurrence of the pellagrous rash after long intervals and stated that one man entered the asylum without any signs of pellagra and it was fifteen years before symptoms reappeared, which they did so severely that the man died. Now, no maize is allowed in the asylum, the flour is regularly analyzed and the bread is baked on the premises.

In 1910, with Drs. Blue, Lavinder and Siler, I examined the family Pavinato of Chiesanova (Padova), consisting of man, wife and five children. The parents were old pellagrins, the children had contracted the disease all at about the same time the year previous on reaching Treponti, a pellagrous locality on the Rialto stream to the north of the Euganean Hills, Padova. Since then I have come across many similar instances of families migrating to an endemic center and all, or the majority of members, in each family becoming affected at about the same time within the first year of residence. Thus, in November, 1911, the family Bruni had moved from Lorina, near Vicenza, to a place called "Contrada Rebecca" in S. Pietro in Gu (Padova). At the beginning of May, 1912, Maria, aged 20; Pasqua, aged 18, and Teresa, aged 7, developed marked pellagra symptoms. The mother, who spent most of her time in the house, showed no signs of the disease.

The influence of meteorological conditions on pellagra is very marked. This year, in Italy, the latter part of the winter having

been exceedingly mild, pellagra broke out much earlier than usual. Later, a cold spell put an end to it at a time when, under ordinary circumstances, it would have been most prevalent.

At Le Cupe, near Abbadia di Petroja (Perugia), I examined the family Anselmi, composed of ten members. The head of the family, Pasquale, aged 55, had suffered from the disease in former years. At present he seems robust and healthy. His wife, Camilla, aged 50, said that every spring during the last five years she had suffered from marked erythema and giddiness. Her eldest son, aged 28, lived in France and was healthy; her second son, who drove the laboring oxen, was likewise healthy; the third son, aged 15, had been a pellagrin during the last five years, the erythema occurring always in May; the fourth son, aged 11, had also been a pellagrin during the last four or five years, his eruption appearing likewise in May; the daughter, aged 9, had suffered from pellagra during the last four years, and her rash appeared always in April; the wife of the eldest son, aged 24, had come to live at the Cupe only three years ago, and last year, after parturition, she developed pellagra; her baby also developed pellagra at the same time when only three months old; the wife of the second son stated that she had been a pellagrin since childhood, and that her rash appeared invariably in April. Here were, in one family, several pellagrins all living in the same house, working in the same place and partaking of the same food, some exhibiting the pellagrous eruption *always in April, others always in May*. This difference and constancy in the month of recurrence of the pellagrous symptoms in the various members was pointed out by the patients themselves, who had been struck by its peculiarity.

Everywhere I have endeavored to ascertain the relative incidence of the disease in the two sexes. I have found that it varies somewhat from place to place in accordance with peculiar topographic conditions and with the local working habits of the people. The reason of the greater prevalence in women, in most places, is obvious enough: the women are in touch with the streams far more frequently than men, fetching water, washing clothes, tending animals. In my drives through the country, I have always seen the women at the streams.

The long and well ascertained immunity of towns was repeatedly confirmed in all the countries visited and so also the immunity

of the Jews, who never engage in field work. For the same reason of occupation, gypsies were found to be immune in Hungary, but not always in Roumania, where they are far more numerous and fully exposed to the infective agency.

In Oviedo (Austrias), where Casal first recognized pellagra, a very remarkable fact was pointed out to me: Two streams, the Nora and the Nalon, run through the district in the same direction. In the days of Casal pellagra occurred along both these streams. At the present day, the disease is limited to the banks of the Nora, not extending, according to Dr. Sarandeses, for more than two or three kilometers on either side. Both Dr. Valdes, Health Officer of Oveido, and Dr. Sarandeses assured me that cases along the Nalon are now either extremely rare or totally absent, whilst, about thirty years ago, they were still very common. They could not ascertain this curious but well ascertained fact with any of the pellagra theories known to them. I was soon able to discover that a great change had taken place. Several industrial establishments have risen along the Nalon, polluting its waters with anthracite waste products and thus killing off all fish and other forms of animal life. The Nora instead has remained in its natural condition, and I found it teeming with Simuliidæ. Together with Dr. Chalmers and Dr. Angel Magnet, Medico de la Beneficencia provincial, I visited the Pueblos of Lugones Naon, Viella and Folgueras and saw several interesting cases of pellagra. The Austrian peasants believe that the disease is acquired along the streams and that it is caused by the morning and evening moisture (orbayn), a popular belief analogous to that which long prevailed concerning malaria. At Folgueras the very first woman we met—Dolores Menendez[2]—was a pellagrin. She told us her illness broke out four or five days after her last confinement. Her friends had warned her to beware of the neighborhood of the Rio. At a small inn opposite the station of Collotto, the host, Don Juan Emanuel Luavez, told us that the mall de la rosa lurks along the rios in the shape of mist. The disease causes tristezza and those who are struck by it are compelled to return to the rio and die in the waters which brought about the illness. He told us of a woman who, not long ago, threw herself from the bridge into the Nora, and "not only this senora," he added, "but various."

In the French Landes, we found that pellagra has become exceedingly rare, but it is very important to notice that malaria has likewise almost entirely disappeared from the same region. About fifty years ago, both pellagra and malaria were rampant; now a case of either disease is looked upon as a great rarity. The simultaneous regression of pellagra and malaria has been brought about by the same causes, viz., improved drainage, intense cultivation, greater prosperity and last, but not least, the introduction of great quantities of fish in all the streams and other water bodies. In the case of the Anopheles-conveyed malarial infection, we can readily understand the operation of these improvements introduced not for the purpose of combatting disease, but only for agricultural and economic reasons. To my mind, the simultaneous rise and fall of both malaria and pellagra under identical surrounding conditions is a fact which tends to corroborate the view of a similar etiology in both diseases.

In the valleys of the Austrian Tyrol, the connection between stream and disease was well apparent and Simuliidæ abounded. Dr. Weiss, the government pellagra inspector, who took part in our excursions, was greatly impressed. Last April, in Rome, at the time of the International Dermatological Congress, I was informed by Dr. Kutchera, principal medical officer of the Tyrol, that Dr. Weiss, after a year's careful work, was fully in agreement with my views.

In Roumania, the connection was also very evident. The Roumanian peasants say that in old standing cases the pellagrous rash and other symptoms recur each year in March at the time "when the new grass begins to sprout" (O data cu coltue ierbei), but that in new cases the signs always appear later, viz., in April or May. This popular experience, confirmed by the physicians, is of interest in view of the insect-borne theory of the disease. In malaria the relapses in old cases occur long before the appearance of fever paroxysms in new cases, the intervening period being that in which the mosquito cycle takes place.

In Bucarest I was told that close to the Bulgarian frontier, in the village of Hotarele, inhabited by Roumanians and Bulgarians, pellagra was very prevalent amongst the maize-eating Roumanians and altogether unknown amongst the Bulgarians, who do not eat maize. I asked to be taken to Hotarele and on arrival the local physicians,

Drs. Braun and Gadescu, showed me at once a number of Bulgarians with marked pellagra symptoms. The statement made with so much confidence in Bucarest was absolutely foundless in Hotarele, but what a splendid tidbit for the easy-chair zeist, who relies for his facts on second-hand information!

The most interesting and suggestive observation I was able to make refers to pellagra in the islands of the Venetian Lagoon. Venice, with its urban population, is, as is well known, totally free of pellagra. The island of Lido, opposite, is immune. Murano, close by, with its industrial population of world famous glass blowers, is also quite free. The islands that harbor pellagrins are: Palestrina and Chioggia, between Lido and the mainland to the south, about the mouths of the Brenta and Adige rivers, and the group of islets formed by Burano, Torcello, Mazzorbo, S. Erasmo, etc., between Lido and the mainland to the north, about the mouth of the Piave River. Both Pellestrina and the Burano group of islets are inhabited by fishermen who fish in various parts of the lagoon and, not infrequently, along the mainland coast.

Burano is a small island entirely covered by closely clustered houses. There is not a single field or garden in the whole place. As a town, one would naturally expect it to be entirely free from pellagra just like the neighboring islands of Venice and Murano, instead of which a large proportion of its inhabitants are pellagrins. When I visited the island, together with Dr. Chalmers and the two government physicians, Belli and Jachina, I had not been ten minutes in the piazzetta, waiting for the local health officer, before meeting three men and a boy exhibiting very marked pellagra symptoms. The local physician informed me that *the Burano pellagrins are almost exclusively males,* women pellagrins are quite exceptional. He had never seen the disease in very young children. *His youngest cases were boys from ten to twelve years of age.* He took us to see a man he was about to send to the pellagrosario of Mogliano Veneto. This man—Leopoldo Trevisan—59 years of age, was a fisherman and a native of Burano. From March to May he fished along the mainland coast south of Fusina, sleeping at night in a stable at Gambarare di Mira. Coasting the "barena" and especially in places near outflows of sweet water he had been attacked and pricked by "mosciolini," minute flies, which appeared at sunrise and more frequently in the evening towards sunset. At

Cavà Zuccherina
Piave R.
Torcello
Mazzorbo
Burano
Name of River not given on original
Canale Brenta
Murano
Tre Ponti
Gambarare
Venice
Fusina
Lido
Pellestrina
Chioggia
Brenta R.
Adige ...

Burano there were plenty of mosquitoes, but he had never seen the "musciolini" of the Brenta waters. From June to February he fished near Burano, sleeping at home in winter, in his boat during summer. His son had also been to Gambarare and was likewise a pellagrin. Of the thirty men who fished with him, the majority were pellagrins.

The Burano fishermen, like all Venetian peasants and laborers, eat a great deal of polenta, but *they buy their maize flour in Venice, where there is no pellagra.*

A number of Burano men work at the arsenal in Venice; not one of these has ever presented the slightest sign of pellagra. Every day these men take with them a slice of their homemade polenta for their midday meal.

In the neighboring island of Mazzorbo there are many vegetable gardens, and the population of the island is made up partly of fishermen and partly of gardeners. The fishermen, who frequently leave the island and go to fish along the mainland coast, contract pellagra; the gardeners who work on the island, though engaged in field labor, are immune.

These observations led me to carefully examine the whole of the mainland coast embracing the lagoon. I found pellagra prevalent all along the coast and Simuliidæ abundant in all the rivers and in many of the streams. It is obvious, therefore, that the Burano and Mazzorbo fishermen contract the disease whilst fishing along the coast. This explains why, contrary to the general rule, the disease in these islands is restricted almost entirely to adult males and to boys above ten who accompany their fathers in fishing expeditions. It explains the immunity of the Mazzorbo gardeners and of those Burano men who work in the Venice arsenal. It explains the immunity of the Burano women and girls who stop in the island to work at that wonderful needle-made lace, the "punta in aria," for which the island has been at all times famous. It explains the exceptional occurrence of the disease in the very few women who go and do field work on the mainland. Indeed, I think it would be difficult to find a more convincing array of facts in favor of the insect-borne theory of pellagra.

Along the coast, I found pellagra again more prevalent in women and again I saw it in infants and very young children. Thus at Cavazuccherina, at a place called the Cristo, I found the family

Longata with four pellagrin children, and the family Berto with no less than six pellagrin children, the youngest fourteen months old.

In the narrow, dike-like island of Pellestrina the conditions appear to be somewhat different. Nearly one-third of the cases are in women and there are two or three cases in children seven to nine years of age who are said to have never been out of the island. There are no streams in the island and infection, if really local, can only take place by means of wind-carried insects. In the same island also malaria has been observed in children who had never been out of the island, and the local physician told me that Anophelinæ are not indigenous, but that they suddenly appear and as suddenly disappear with certain winds.

Quite recently Dr. Chalmers and Major Belli visited the island of Palestrina. Dr. Chalmers sent me a long and interesting report of his investigations. He concludes: "The Major and myself consider that the evidence collected strongly supports your view. What we have seen is strongly against the maize theory and strongly in favor of an infection and not an intoxication. It appears to us more probable that the usual mode of infection is indirect and by means of a biting fly."

So far, all my experience is strongly in favor of the Simuliidæ as carriers of the pellagra germ. It is possible, however, that the true criminal may turn out to be Leptoconops or some species of Geratopogon with aquatic larva and habits similar to those of Simuilum. Of course, if Simulium is really absent from Lower Egypt, it must be so for that country at any rate, but I doubt it. Unfortunately so little is known concerning the smaller biting flies that it is impossible to make any reasonable surmise.

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SPECIAL POINTS OF EPIDEMOLOGICAL INTEREST IN PELLAGRA.

By L. W. SAMBON, London, England.

I regret that I am prevented from accepting your very courteous invitation to attend the Second Triennial Meeting of the American Association for the Study of Pellagra. I also regret that owing to pressure of work (unfortunately not pellagra work) I have been unable to prepare a paper.

I have been following the progress of American pellagra investigation with interest and expectation, because I know what power of knowledge, ability, wisdom and determination you can bring to bear on anything you take up on your side of the Atlantic.

Pellagra is no new disease in the United States. Centuries alone can explain its wide range extending from the Atlantic to the Pacific Ocean and from the Gulf Coast to the Great Lakes. Yet, until five or six years ago, notwithstanding the recognition of a few isolated cases, such as those of Davis in 1834, of Gray and of Tyler in 1864, this grave endemic malady had been overlooked in North America, just as it had been overlooked in Spain before Casal, in Italy before Pujati, in France before Hameau, in Egypt before Pruner.

The late recognition of pellagra in the United States, notwithstanding the wide distribution of the disease within its boundaries, is most instructive when compared with the history of the recognition of the malady in Italy at the close of the eighteenth century, because pellagra, in the days of Frapolli, was also widely distributed throughout north and central Italy, and occupied, amongst the foothills of the Alps and Appennines, the very same localities in which it is now stationed. I wish to draw very particularly your attention to this important topographic fact, because the great majority of Italian physicians, hopelessly imbued with the maize idea, still persist in believing that pellagra was a new disease to their country when first described, at Milan, in 1771.

The failure to recognize pellagra in the United States at an earlier date is no disparagement to the American physician—a rec-

ognized leader in matters medical—because the reason is one inherent to the disease itself. Pellagra is an insidious, protean disease which, like plague, spotted fever, malaria and other infectious diseases, may lie epidemically dormant for many years and then, under favorable œcological conditions, become once more rampant.

What strikes me very forcibly is not the lateness in recognizing the disease, but the prompt and able way you have grappled with this many-headed scourge. Since Babcock and Watson raised the alarm in 1907, already two conferences on pellagra have been held in Columbia, under the auspices of the enlightened and praiseworthy State Board of Health of South Carolina, and a third conference is now convened.

At the time of the first conference of 1908, practically nothing was known of the distribution and epidemiology of pellagra in the United States and you were equally divided between the yearling protozoan theory and the centenarian corn belief. At the time of the second conference of 1909, your epidemiological experience of pellagra was very limited, but you had read the literature and you were decidedly under the influence of "zeism." Today you come to the third meeting with your own ideas, based on facts observed by yourselves in your own surroundings, and I feel sure the results of this conference will greatly advance the elucidation of the true cause of pellagra and thus lead to the vanquishment of one of the most widespread and fearful of disease scourges.

During the last two years, thanks to Mr. Henry S. Wellcome, a friend whose interest in science and munificence have greatly contributed to the advancement of medical research, I have been able to visit the most important pellagra districts of Spain, southwest France, south Tyrol, north and central Italy, Transylvania, and Rumania. I had the good fortune of being accompanied in my peregrinations and assisted in my researches by Professor Albert A. Chalmers, whose splendid textbook on Tropical Diseases, written conjointly with Castellani, is known to all. The amount of information collected is considerable and most interesting, but, unfortunately, unavoidable circumstances have retarded its publication.

Allow me to draw your attention to one or two points of epidemiological interest which I hope will be discussed at your meeting.

GEOGRAPHIC AND TOPOGRAPHICAL DISTRIBUTION.

Two years ago in my "Progress Report" I pointed out that pellagra is essentially a disease of the banks of swift-flowing streams. Its preference for the torrential stream explains why it is more prevalent in the foreland or "Piedmont Section" of mountain ranges, but it is found also in the flood plains and delta districts of great rivers about the distributaries of the main stream.

In Eurasia pellagra extends throughout the Alpine-Himalayan system, occupying, never the high mountains, but always the river valleys of the foreland. I have made a very careful study of the distribution of the disease in the Tyrol and northern Italy and I have followed some of the rivers, such as the Brenta and Piave, for instance, from source to mouth.

It is gratifying to me to learn that in the United States Professor Roberts, Drs. Wood, Grimm, Morse, Johnson, Elrod and others have already confirmed my topographic findings. Evidently in Georgia and the Carolinas pellagra is limited to the Piedmont section of the Appalachian system.

Since my paper of 1905, much has been added to our knowledge of the geographic distribution of pellagra. I need but mention its recognition in the United States and in Nyasaland. Yet I believe the disease has a much wider range. My researches and inquiries lead me to believe that it is present in many other countries, as, for instance, in India at the base of the Himalaya, in Scotland, in the north of England, in the Shetland Islands, in southern Italy and Sicily. For many of these places we have already a few isolated records of indisputable cases of local origin.

I also wish to point out that pellagra has not entirely disappeared from the South of France, as Regis and Marie led us to believe. It is certainly far less prevalent, but cases do occur, not only in the Pyrenean region, but also in the Landes along both the Leyre and the Ciron Rivers, with their tributaries, the valleys of which have been, from the days of Hameau, and probably long before, its chief Gascony centers.

DISTRIBUTIONAL CONTRAST BETWEEN PELLAGRA AND MALARIA.

From an early date, Italian physicians have spoken of antagonism, distributional and clinical, between pellagra and malaria. More recently, Robolotti wrote: "Both my observations and the official

statistics prove that pellagra is absent from, indeed, I might say, opposed to, swampy districts in which the intermittent fevers prevail."

I have seen both pellagra and malaria in the same district and in the same individual, but, certainly, the topographic distribution of the two diseases is quite different, indeed, though the relative distributional areas of pellagra and malaria do overlap in a few places, they are decidedly inverse. Pellagra prevails chiefly in the highlands trenched by swift-flowing streams, malaria prevails in the swampy lowlands. A glance at the enclosed maps showing the relative distribution of pellagra and malaria in Italy will suffice to impress the contrast.

RECURRENCES.

A fact to which I attach great importance on account of the light it throws upon the etiology of the disease is that of the "recurrence" of the characteristic dermatitis and other symptoms every spring until the patient either recovers, subdues the disease or dies. These recurrences continue to occur in patients far removed from the place of infection and placed in asylums in which not only their surroundings are completely changed, but also their food and other habits.

Two years ago, I took over to London a young pellagrin girl of Promano, a pellagrous locality near Citta di Castello, Perugia. This patient had had the disease since childhood and her mother, also a pellagrin, had committed suicide during a period of recurrence. Nunziata Betacchioli—such is her name—has lived for two years in London, in my house, acting as nursery maid. The change of food and life habits has greatly improved her physique. She looks the picture of health and yet, in the spring of 1911, and again this year, early in April, she exhibited the usual recurrence, presenting: weakness, headache, vertigo, strangeness of behavior and desquamation of the epidermis on the dorsum of hands and feet and also on legs and forearms, especially about the knees and elbows.

The pellagra recurrences are in every way analogous to the recurrences which occur in malarial subjects. By malarial recurrences I do not intend malarial relapses, that is to say, fever paroxysms occurring at short intervals during the epidemic season, but the seasonal return to activity of the malarial parasites after their winter

latency or "hibernation." It is this seasonal revivement of the Plasmodiidæ, in old malarial subjects, that insures the continuance and dissemination of the disease. Every year we notice first a veritable efflorescence of recurrences in the old cases, at the season in which the new mosquito brood begins to assume the imago stage, then, after an interval during which the parasitic legions undergo sporogony within their insect hosts, the new cases begin to crop up more and more numerous.

The very same thing occurs in pellagra. In the first place we have the recurrence, that is to say, the revivement of the disease causitive agent, in old cases, occurring always in spring, sometimes a little earlier, sometimes a little later, according to the more or less favorable meteorological conditions, then, later in the season, commence to appear the new cases.

Having made this observation in Italy, in 1910, I was delighted to learn, the year after, in Bukarest, that I had only just discovered a fact long known to the Rumanian peasantry. Drs. Lupu and Mironescu told me the peasants know very well that in old cases the pellagrous eruption, *"O data cu coltue ierbei,"* that is to say, appears in March with "the sprouting of the new grass" and that in new cases it occurs always later in April, May or even June.

INFECTION OF NEW ARRIVALS.

A most important epidemiological fact which came several times under my observation is that of the infection of persons recently settled in a pellagrous locality. The infection usually takes place within the first year of residence, in the epidemic season, soon after exposure to the specific infective agent. In my "Progress Report" I gave a few examples, such as that of the Pavinato family seen at Chiesanuova, near Padua, in the presence of Surgeon General Rupert Blue, Captain Siler and Dr. Lavinder. The Pavinato family consisted of man, wife and five children. The parents were apparently healthy, but the five children presented very evident signs of pellagra. The eldest child was thirteen years old, the youngest about two. All had contracted the disease, in the spring of the previous year, soon after reaching Treponti, a pellagrous locality in the Euganean Hills, Padua.

The same year, at the Pellagrosario of Citta di Castello, I had the opportunity of examining Veronica Pierini and her seven-month-

old babe, both pellagrins. The mother had contracted the disease the previous year, soon after moving from a healthy village in the Appennines to Passano on the stream of the same name.

In November, 1911, the family Bruni moved from Lerina, near Vicenza, to a place called Contrada Robecca in S. Pietro in Gu, Padua. Early in May this year three out of its four members had developed marked pellagra symptoms.

At a place called Pugliola, on the stream Puglia, Province of Perugia, Drs. Magnini and Lupatelli took me to see a boy eight years old who had been born and nursed in prison until he was five months old, then sent to the Pugliola for fosterage in March, 1903. Here he contracted severe pellagra within two weeks of arrival.

In 1910, together with Professor Balp and Captain Siler, I went to Castione della Presolana, a mountain district 870 meters above sea level, where over ninety cases of pellagra had been notified by the local authorities. I examined a number of these pellagrins and found that they were for the most part adults and above middle age. The children were all healthy looking. Some of the patients I questioned had contracted the disease only two, three, or five years before, others stated that they had had it for ten, twenty or even thirty and more years. I soon discovered that Castione is not a pellagrous locality, notwithstanding that a large proportion of its adult population suffers from pellagra. The people of Castione are in the habit of descending into the neighboring province of Brescia twice every year, in spring and autumn, to undertake various field labors or the rearing of silkworms, and I found that in many cases the date of infection coincided with that in which the patient first went to work in Brescia.

One of these patients—Giovanni Ferrario—a powerfully built man, sixty-three years of age, had worked as a miner in France and Prussia most of his life. Eight years ago, he gave up mining and bought some land in the province of Brescia. There he contracted the disease the very first year he went to work on his own property. When I saw him he was just recovering from the fifth recurrence. This man had two sons, both had contracted pellagra many years before their father. They had likewise contracted it in the province of Brescia, whither they had gone together to take up field labor, one of them being eleven, the other nine years old

at the time. Their mother and sister, who had never been out of Castione, had always been perfectly well.

Balardini (1860) states that, according to Dr. Calotti of Borgonato and Dr. Ferrari of Orizinovi, the Tyrolese mountaineers who used to come to Lombardy in winter and returned to their mountains early in spring, escaped pellagra, whilst those who remained to work in the fields and adopted the food habits of the Italian peasants, "after one year or little more contracted our disease."

Cerri (1850) saw the disease in French soldiers who had contracted it in Italy during the Napoleonic invasion, and Gustave Hameau (1853) described it in another French soldier who had contracted it in Algeria.

These and many other cases which I might quote, show very clearly that healthy people are liable to contract pellagra on moving into an endemic center of the disease and that infection usually takes place at the very first opportunity.

AGE INCIDENCE—PELLAGRA IN YOUNG CHILDREN.

Pellagra may occur at any age. I have seen it frequently in children under one year of age and in elderly men and women who had contracted it for the first time after their fiftieth year of life. The youngest case I can mention is that of an infant—Luigi Anselmi—who developed the disease in 1911, when only three months old. He lived at Le Cupe, near Abbadia di Petroja, Italy, on a farm skirted by the Nestore, an ideal Simulium stream. At the time of my visit this year he had had his first recurrence and still presented unmistakable evidence of the characteristic dermatitis on face and dorsum of hands. I was sent to see this case by Professor Pisenti, of Perugia, who had had the opportunity of examining it the previous year in the early stage of the eruption. Dr. Chalmers also examined this interesting case.

I have already mentioned Giovanni Ferrario, of Castione, who contracted the disease for the first time in 1904, at the age of fifty-seven. I have seen pellagra in much older people, but without being able to ascertain the exact date of infection. Thus, at Bratto (Bergamo) I saw a pellagrin woman—Caterina Tommasoni—who was eighty-two years old and stated having had the disease since the age of seventeen, a few months after her marriage. Whilst travelling with Dr. Fattore, of Nocera Umbra, I met, on the way to

Costapennacchio, a pellagrin of old standing—Natale Betti—who was ninety-eight years of age, and Dr. Armanni, Health Officer of Assisi, told me of a pellagrin woman in his district who had reached the advanced age of one hundred and two years.

With regard to the age incidence of pellagra there is considerable discordance in literature. A number of authors, both old and recent, assert that the disease is very rare in young children. My personal experience is that children are very liable to contract the disease, indeed, their liability to pellagra is exactly comparable to the liability exhibited towards malaria by the children inhabiting malarious localities. In all active pellagra centers I have found the children affected wholesale. Therefore I do not now consider a place to be a true pellagra station unless I find the disease in very young children who have never been out of the locality.

Besides the three-month-old case already mentioned, I have seen two other infants who were attacked at the ages of four and five months, respectively. Such early cases are somewhat rare, but the disease is quite frequent in children from six to eighteen months old.

In families with numerous children living within the endemic stations of the disease, I have often found both the parents and all the children affected.

At Rivotorto, near Assisi, I examined the family Porticelli, consisting of man, wife, and three children. Parents and children were all pellagrins. The eldest child, a girl seven years old, had contracted the disease in her first year. The second at the age of three, after an attack of pneumonia. The youngest, in September, 1909, when about eight months old. At harvesting time, between June and September, the whole family go and encamp on the banks of the Ose, a stream in which my assistant, Mr. Amoruso, found an extraordinary number of Simulium flies belonging to the species *Simulium pubescens,* Macq.

Not far from the Porticellis lived the family Ceccotti, consisting of man, wife and four children, likewise all pellagrins. The eldest child, 11 years old, had developed the disease at the age of four years. The youngest, born on the 13th of July, 1911, had contracted it in March, 1912.

At Morra, near Citta di Castello, I inspected the family Corneli, consisting of man, wife and five children. All were pellagrins save

the four-month-old infant. The second had contracted the disease when eleven months old and still at the breast.

At a place called Salsi, near Gavazuccherina, Venice, I was taken to see the family Berto, consisting of man, wife and six children, the youngest fourteen months old. All were pellagrins. Close by lived the family Longato; parents and four children all pellagrins.

At Busa di Tramonto, in the Comune of Teolo, Padua, I saw Silvio Libero with his four young children, all pellagrins.

At Chirignano, near Mestre, Venice, the five children of the family Vescovo were all pellagrins and were sent, with their mother, to the Pellagrosario of Mogliano Veneto.

At Case Volpe, Cura del Paradiso, near S. Presto, Perugia, I inspected the family Luigi Caporale, consisting of man, wife and five children, the youngest ten months old, all pellagrins, and, on the same farm, the family Domenico Caporale with two children two and a half and one years, respectively, all pellagrins.

At Oltre Brenta, opposite the village of Novaledo, in the Brenta Valley, Austrian Tyrol, I saw a family living close to the river with no less than eight children, all pellagrins.

The reason why the majority of authors have considered pellagra to be a rare disease in children is threefold. In the first place many have looked for it, and of course failed to find it, in localities inhabited by pellagrins, but devoid of the necessary transmitting agent and, therefore, not giving rise to new cases. Secondly, the little patients are seldom, if ever, brought to the physician, and thirdly, the disease escapes observation or recognition, being frequently very mild and of short duration in children.

When we consider how seldom adult pellagrins seek the physician, especially in the early stages of the disease, it will not be surprising that they do not bring their children whom they believe merely sunburnt. Even when the children are very seriously affected they do not bring them to the doctor, preferring to treat them themselves according to their own notions.

At la Rogara, on the road between Abbadia di Petroja and Trestina, quite accidentally, I came across a most interesting case in a child two and a half years of age. This child had contracted the infection in 1911 and had been seized by a severe recurrence on the first of March last. The mother—Madalena Berardinelli—told me that the child had had fever for over a week, that he had obstinately

refused all food, that he was greatly prostrate and presented marked swelling of face, hands and feet. The feet were so much swollen that he could not wear his boots. Notwithstanding the gravity of the case, the local doctor, who lived less than a mile away, had never been called or informed. When I saw him in the presence of Dr. Chalmers and the local health officer, he still presented all the signs of a severe infection.

I have seen many severe cases of pellagra in children. Some presented an extensive dermatitis involving the whole of the face, the hands, wrists, feet and neck, others pronounced nervous symptoms. Amongst the first, striking examples were: Olga Selmin, of Galzignano, aged six, who was first attacked in May, 1911, and developed a very severe and extensive eruption in April last. Emilio Bellini, of Volta Barozzo, Pedua, a three-year-old boy with full mask, gloves and boots, and Benedetto Simeone, a four-year-old boy seen at Grumese, Austrian Tyrol. In the Pellagrosario of Roman, Rumania, Dr. Vasilu showed me an interesting and severe case in a five-year-old girl from Stenita. A sister and an aunt of this child were also in the asylum for the same complaint. At the Pellagrosario of Mogliano Veneto, Dr. Caldara showed me Anastasia Simion of Martellago, a five-year-old child, who had contracted the disease in her first year and showed marked nervous symptoms. This year the eruption had recurred early in January. Grave nervous symptoms have been noticed in children in Rumania and in other countries. Dr. Warnock states that in Egypt he has seen scores of children "displaying splendid black pellagrous rashes and usually insane."

During my field investigations, I made it a special point to look for the disease in children and I found it again and again in districts in which the local health officers had assured me of its absence or extreme rarity. I looked for pellagra in very young children not only for the reason of ascertaining its prevalence in early childhood, but, more especially, to understand a number of epidemiological facts which become obscured in adult and elderly pellagrins who often change residence, are encumbered with additional infections, and seldom can give the exact date at which they contracted pellagra.

Whilst the majority of authors have hitherto looked upon pellagra as a rare disease in children, a few have admitted the possibility

and looked upon it as evidence of hereditary transmission. It is with this idea in mind that some authors have even gone so far as to assert that children may be born with the pathognomonic signs of the disease. Thus Zecchinelli (1818) says: "Children of two or three years are affected, and cases of pellagrin infants at the breast are not lacking. Some cases, though exceedingly rare, have been reported of infants being born with manifest pellagra."

I have never seen and I have never heard of a single case of congenital pellagra, neither have I been able to find in literature any first hand and authentic record of a case. I have no reason to believe the possibility of placental transmission during fœtal life, but, if it does ever occur, it must be exceedingly rare and certainly all my experience, so far, is against it. In malaria, likewise, transmission during fœtal life has been asserted, and a few cases looked upon as doubtful, have been mentioned, but the mass of experience is against it.

IMMUNITY.

My experience inclines me to believe that a certain kind of immunity is acquired in pellagra by those resident in pellagrous localities. This immunity, acquired especially in childhood, is shown, I think, by the fact that, within its endemic stations, the disease is very prevalent in young children, less in older children and adults. Then again fatigue, starvation, exposure to meteorologic inclemences and intercurrent diseases invariably revive the latent infection or predispose to reinfection those resident in pellagrous stations, just as they reawaken fever paroxysms in the inhabitants of malarious localities.

PELLAGRA IN THE ISLANDS OF THE VENETIAN LAGOON.

The most interesting and suggestive observation I have been able to make refers to the incidence of pellagra amongst the inhabitants of the various islands of the Venetian Lagoon.

Venice, with its urban population, is, like all other large towns in pellagrous countires, entirely immune. From time to time exceptional cases have been notified, but they invariably occurred in persons immigrated from the rural districts of the province, where they had no doubt contracted the disease.

The island of Lido, just opposite Venice and facing the Adriatic, is likewise immune.

Murano, close by, with its industrial population of world-famed glass-blowers, is also quite free from pellagra.

The islands that harbor pellagrins are: Pellestrina and Chioggia, between Lido and the mainland to the south, round the mouths of the Brenta, Gorzone and Adige rivers, and the group of islets formed by Burano, Mazzorbo, Torcello, S. Erasmo, etc., between Lido and the mainland to the north about the mouths of the rivers Sile, Piave, and Livenza.

Both Pellestrina and the Burano group of islets are inhabited chiefly by fishermen who fish in various parts of the Lagoon, and, not infrequently, along the coast of the mainland.

Burano is a small islet entirely covered by closely clustered houses. There is not a single field or garden in the whole place. As a town, one would expect it to be entirely free from pellagra, just like the neighboring town islands of Venice and Murano, because there is nothing better ascertained and more unanimously accepted in pellagra than the immunity of cities, instead of which a considerable proportion of the inhabitants of Burano are pellagrins.

When I visited the island, in the company of Dr. Chalmers, Professor Belli, and Dr. Jachina, I had not been ten minutes in the piazzetta, waiting for the arrival of the local health officer, before observing three men and one boy exhibiting very marked pellagra symptoms. From the local physician I elicited that the Burano pellagrins are almost exclusively males, female pellagrins being altogether exceptional. The disease is never seen in very young children, the youngest cases the local doctor could remember being boys from ten to twelve years old.

The presence of pellagra in the streamless islets of the Venetian Lagoon had been put forward as a conclusive argument against my Simulium theory, it is now, I believe, one of the strongest in its favor. The absence of pellagra in young children proved that the island was no endemic center, and this was corroborated by the almost exclusive limitation of the disease to the adult male population, a most striking and important epidemiological fact when we consider that in all pellagrous localities throughout the world the disease is decidedly more prevalent in women. Indeed, this greater prevalence in the female sex is, as Professor Roberts states in his

recent and masterly work on pellagra, "one of the striking features of the disease."

The explanation of the limitation of pellagra to the men of Burano was soon discovered. The local physician took me to see a pellagrin he was about to send to the Pellagrosario of Mogliano Veneto. This man—Leopoldo Trevisan—59 years of age, was a fisherman and a native of Burano. From March to May he was in the habit of fishing along the coast of the mainland south of Fusina, sleeping at night in a stable at Gambarare di Mira. He told me that whilst coasting the barene, and especially in places near outflows of the Brenta waters (Naviglio di Brenta) and other small streams between Burano and Fusina, he had been frequently attacked by "mosciolini," minute flies which appeared about sunrise and perhaps more frequently in the evening towards sunset. At Burano he had seen plenty of mosquitoes, but never the "mosciolini" of the Brenta waters. At other times of the year he fished nearer to Burano, sleeping at home through the winter, in his boat in summer. His son, who had accompanied him once to Gambarare, was also a pellagrin, and so were the majority of the thirty-odd fishermen who worked with him.

The Burano fisherman, like all Venetian peasants and laborers, eat a great deal of polenta. They buy their maize-flour in Venice, where pellagra is unknown, and they eat it with their wives and children, who do not suffer from the disease.

A number of Burano men are artisans; they go every day to work at the Venice arsenal. Professor Belli told me that pellagra is quite unknown amongst them. They invariably take with them a slice of the homemade polenta to eat at their midday meal.

The women and girls of Burano remain in the island to work at that wonderful needle-made lace, the "punto-in-aria," for which the island has been in all times famous. Pellagra is unknown among them. Only very few cases of the disease are known to occur in the Burano women, and such are found to be limited to women who periodically leave the island to do field work at either S. Erasmo, or at Treporti and other places on the adjoining mainland.

In the neighboring island of Mazzorbo there are many vegetable gardens, and the population of the island is made up partly of fishermen and partly of gardeners. The fishermen, who leave the

island to go fishing along the mainland coast, contract the disease; the gardeners, who remain on the island, are said to be immune.

These observations led me to carefully examine the whole of the mainland coast, embracing the Lagoon, with the result that I found pellagra more or less prevalent in all the coast districts and Simuliidæ abundant in all the rivers and in many of the streams. On the mainland pellagra was again more prevalent in women than men, and again I saw it in infants and very young children.

It is quite obvious, therefore, that the Burano fishermen contract the disease whilst fishing along the mainland coast. This explains why, contrary to the general rule, pellagra in this island is restricted almost entirely to adult males and to boys above 10 years of age who begin to accompany their fathers in fishing expeditions. It explains the immunity of the Mazzorbo gardeners and of those Burano men who go to work at the Venice Arsenal. It explains the immunity of the Burano women and girls employed in the island at lace-making. It explains the exceptional occurrence of the disease in the very few women who go to do field labor on the mainland. (Dr. Chalmers and Professor Belli, who made a thorough house-to-house visitation, could only find three cases.) It excludes any idea of direct contagion, either by contact or sexual intercourse. It excludes house infection and direct aerial conveyance. It disposes of the maize hypothesis, and it overthrows the belief in hereditary transmission—a belief which, strange to say, is held by the majority of "zeists." Indeed, it would be difficult to find a more convincing array of facts in favor of the insect-borne theory of pellagra.

In the narrow, dyke-like island of Pellestrina the conditions appear to be somewhat different. Here nearly one-third of the cases are in women and there are a few cases in children from 7 to 9 years of age who are said never to have been out of the island. There are no streams in Pellestrina any more than in Burano, and infection, if really local, can take place only by means of wind-carried insects. In the same island also malaria has been observed in children who have never been out of the island, and the local physician told me in 1911, that Anophelinæ are not indigenous, but that they suddenly appear and as suddenly disappear with certain winds. Drs. Chalmers and Belli, who visited the island quite

recently, found that there are more cases in the village of Pellestrina, which is nearest the mainland, than in that of S. Pietro, which is farthest.

PARASITE.

In 1911, together with Dr. Chalmers, I found a new photozoal organism in the brain and spinal cord of a young Rumanian peasant who died of acute pellagra in the Pellagrosario of Roman, the very moment we entered the institution. The autopsy was made by Dr. Chalmers within one hour of death. The parasite found in the smears has been examined by Sir Patrick Manson, Sir William Leishman, Professor Minchin, Dr. Low, Professor Laveran, Drs. Mesnil, Brumpt, Nattan-Larier and by other competent protozoologists, and the general opinion is that the organism is probably of protozoal nature.

At a meeting of the London Society of Tropical Medicine and Hygiene, Sir William Leishman said: "Dr. Sambon and Dr. Chalmers have been good enough to show me some specimens of the bodies which they have found in a case of pellagra and I am quite in accord with these gentlemen in considering that they are probably of protozoal nature, though I also agree with them in the guarded manner in which they have spoken of their possible causative role in the disease. Their epidemiological observations are most interesting and appeared to strengthen considerably the theory of Simulium transmission."

The organism appeared to be invariably enclosed in a matrix staining like nuclear material. It resembles the rounded endoglobular forms of certain flagellates.

CAN PELLAGRA BE A DISEASE DUE TO DEFICIENCY IN NUTRITION?

By F. M. SANDWITH, M. D., F. R. C. P., Gresham Professor of Physic, Physician to the Albert Dock Hospital, Lecturer at the London School of Tropical Medicine, Vice President of the Tropical Section of the International Medical Congress for 1913, Honorary Member of the American Society of Tropical Medicine, and Consulting Physician to Kasr-el-Ainy Hospital, Cairo.

It hardly seems three years ago since I was courteously invited to contribute an introductory paper to the National Conference of 1909, and now I have again been desired either to attend or, at least, to send a brief communication to the second triennial meeting of the National Association for the Study of Pellagra.

My plea that I no longer live in a pellagrous country has been answered by the conveners of this conference in a way which makes it impossible for me to decline their later invitation.

Three years ago I concluded my few introductory remarks by saying: "We are now waiting, in the confident hope that some of the pellagra problems, so long unsolved, may be successfully mastered in the United States."

What is the state of our knowledge now? Are we any nearer arriving at the *causa causans?*

If I may judge by more than one hundred reprints of new pamphlets which have been most generously forwarded to me from the United States, there has been no lack of recent literature dealing with pellagra in the English tongue.

High praise may be accorded, in my opinion, to Dr. C. H. Lavinder for the useful précis of our existing knowledge in 1911

We are fortunate now in possessing three books on pellagra in our own language: the American translation from the French of Dr. A. Marie's work, with many additions and illustrations furnished by Dr. J. W. Babcock and Dr. C. H. Lavinder, both of whom have been prominent pioneers in awakening the interest of the medical profession in the United States to the importance of the disease; and this was quickly followed by books by Professor

George M. Niles and Professor Stewart M. Roberts, both of Atlanta. And I understand at least two other works on pellagra have been announced, one by Dr. H. F. Harris and one by Dr. E. J. Wood, while to Dr. George A. Zeller and others we are indebted for a series of admirable photographs.

But the production of books and pamplets alone will not help us to solve mysteries. What we obviously need is prolonged study which bears upon the co-relation of the epidemiology of pellagra with its pathology, and especially with bio-chemistry.

I am not aware that as yet much has been done in the way of examining pellagrous brains and spinal cords by pathologists, accustomed to modern neurological research, nor have I seen many records of the examination of the cerebro-spinal fluid of the living by lumbar puncture.

Light will surely be thrown on the etiology of this elusive disease by such systematic and well organized work as that of the Thompson-McFadden Pellagra Commission, for details of which I am indebted to Captain Joseph F. Siler.

Most of us are still sitting on the fence, waiting till workers prove whether the disease is caused by the ingestion of bad maize or whether Dr. Sambon's theory is correct that the poisonous symptoms are due to something conveyed to man by a biting insect.

One of the arguments brought forward in favor of this theory is that pellagra sometimes occurs in those who have never eaten maize. Surely this point could be elucidated by exhibiting at a pellagra conference, under the eyes of approved experts, five or ten children or adults who are undoubtedly suffering from pellagrous manifestations (such as skin, tongue and knee-jerk), but who are known never to have swallowed Indian corn (*zea mays*) in any form throughout their whole lives? Theoretically one case should be sufficient, but I venture to suggest more, lest sceptics should cavil at the diagnosis. If such pellagrous individuals can be produced, the contention that pellagra is caused entirely by bad maize must fall to the ground, though it would not necessarily prove that diet of some other kind is not the chief factor.

I know that some of my valued correspondents in the Southern States have been very much impressed by the patient and gradual discovery that beri-beri in man and polyneuritis in fowls are caused, not by any poison nor by any microbe, but by too exclusive con-

tinuous use of polished rice. Dr. Braddon's views, though erroneous, put workers again on the right, but abandoned, track; Dr. Grijns, in Java, lent a helping hand and now a young chemist, Dr. Casimir Funk, claims to have determined the chemical composition of the substance, the existence of which was demonstrated by Dr. Fraser and Dr. Stanton. He claims[1] to have isolated this unknown substance which he has christened "vitamine." Though it is so important and vital a constituent of rice as a complete diet, it is only present to the extent of about ten grains to the ton of rice, say one part in 100,000. A pigeon fed on polished rice becomes ill from polyneuritis in about three weeks, yet an almost moribund pigeon can be restored apparently to normal health in eight hours by administering to it a small quantity of "vitamine."

We know from Baron Takaki's experiments in the Japanese navy and from various workers in the Philippines, like Major Weston P. Chamberlain[2] that beri-beri has been eliminated from troops by means of a simple change in their dietary. We know that Norwegian ship beri-beri, which is a peripheral neuritis distinct from but somewhat resembling tropical beri-beri, can be produced by mouldy flour and tinned foods, and can be cured by fresh food to which the sailors themselves, on their return to port, add beer or yeast.

Scurvy, epidemic dropsy and rickets are all diseases due to some deficiency of nutrition, but capable of cure if that deficiency be banished from the diet.

Is pellagra, too, a deficiency disease, waiting for a "Vitamine" to be discovered?

A few years ago Dr. F. G. Hopkins[3] wrote a paper to teach us that a dietary containing zein (*zea mays*) as its only nitrogenous constituent, is unable to maintain growth in young mice, but the addition of tryptophane (an amino-acid absent from the decomposition products of zein) to such a dietary greatly prolongs the survival period of animals fed an zein, and materially adds to the well-being of such animals. It is suggested, in the joint paper from which I quote, that the tryptophane is directly utilized as the normal precursor of some specific "hormone," or other substance essential to the processes of the body.

In Egypt and most other pellagrous countries, it is only the poor maize eater who suffers. The farm laborer who has to support his family on starvation wages, is chiefly attacked; a similar laborer

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earning more regular pay is less victimized, while the farmer and the farmer's domestic servants, who eat the same varied food as their master, entirely escape.

So far as Egypt is concerned, the theory of deficiency of nutrition of spoilt or immature maize, is sufficient, but in the Southern States, where I am told that the pellagra is similar to Egyptian pellagra, we hear of well dressed people contracting the disease in spite of varied diet and easy circumstances!

This unconscious adaptation of the disease to democratic opinion seems to be a fatal blow to the deficiency theory, for it must never be forgotten that the real cause of a disease must prove to be true whenever tested in any country where the disease exists.

Some day soon the mist will clear from before our eyes and we shall all be wondering how we came to be floundering near the goal so long without actually reaching it.

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CONSIDERATIONS AS TO THE ETIOLOGY OF PELLAGRA.

By B. GOSIO, of Rome, and G. ANTONINI, of Milan. Read before the Fifth Italian Pellagra Congress at Bergamo, September 9th, 10th and 11th, 1912, and contributed by its authors to the Second American Conference.

Since the time that the question of etiology has been made a subject of discussion in our pellagra conferences, the present is, perhaps, the first time that uncertainty as to it will appear embarrassing, and resolutions for giving practical advice difficult to form. In all the other conferences the discussion has been, for the most part, limited to questions of scientific detail, and if, at other times, the controversies on single points of interpretation have been lively, the synthetic conclusion was always drawn with unanimity upon the single resolution which in substance may be expressed by the words: "Combat spoiled corn and all its products."

With this war cry the cardinal features of prophylaxis and the spirit of the law advanced harmoniously to success. Therefore their advocates could not be discouraged. But today the most divergent views, after having once invaded scientific territory, will be able to captivate the minds of many, and, what is sadder still, they undermine the foundations of the ancient edifice without presenting reliable elements for the construction of new ones.

Weak points in the doctrine of Lombroso have been noted all along; we, ourselves, have frankly and continuously posted them in high relief; we can also justly say that the conservatives of today were once like messengers sent forward by the great Master himself, only to be pointed out as dangerous raidcals by others.

But the weak points stimulated us to greater scientific accuracy, on the one hand to discover the secret nature of the pellagrogenous poisons, and on the other hand to discern, if, as today many hold, the word pellagra is a broad title which comprehends morbic entities related in some symptom, but distinct in pathogenesis.

Again, there are today doctrines, in great part, entirely opposed to these, which advance threateningly to show the work of the toxico-zeists to be, as it were, absurd, and the struggles, sustained

victoriously through so many years, to be superfluous. And though the mutual contests of the new doctrines are a proof of their weakness, still they have already made many proselytes by suggesting up-to-date ideas to believers in the old creed and by taking advantage of the prestige and attractiveness of novelty.

Let us make a résumé of the present state of the question, so as to count up the forces, and take orientation on the probability of the power of the old doctrine to persist, and of the new, to gain proselytes by its speciousness.

Of the conception of Lombroso there remains much that is positive in the epidemiological and in the experimental field; in the epidemiological field, because always, even up to the very last days, observers worthy of belief have seen pellagra diminish, even to the point of disappearing altogether, with the single modification of the conditions indicated by spoiled corn; in the experimental field, because a great legion of students, still presenting themselves divided in interpretation and in doctrinal formula, always come to find inspiration and support in the same source of facts and proofs which designate the parasites of corn as the recognized cause of the disease, a cause which, up to the present, has enrolled the great majority of forces under a single defensive banner.

But here it is profitable to lay with greater care the foundation upon which, notwithstanding some disunited adjacent parts, we feel we can with confidence maintain the legislative edifice, the Italian law of July 21, 1902.

The use, or rather, the abuse, that is made of corn in rural districts is indisputable; in certain localities the poverty-stricken keep it as their only kind of food.

Furthermore, the fact that this same corn, in various processes, is most easily subject to parasitism by moulds, is also indisputable; nor can the practical importance of this fact be denied or diminished by the negative result of single investigations; and if these should be conducted upon the epidemiological terrain and especially amongst the pellagrous families, they would not succeed in destroying the value of the toxico-zeistic conception, because their pledged character renders them little adequate to the purpose of giving exact scientific data; much more agreeable to this purpose is the generic certainty, recognized by all, of the readiness with which this cereal in its natural state and foods derived from corn, even in sound con-

dition, are subject to alteration. Add to this its daily use as food, generally in great abundance, and one finds one's self compelled to admit with good reason that the results produced in laboratory experiments under artificial conditions also take place when the eater of corn products gradually introduces into his system small quantities of parasitic elements which *in toto* represent a considerable amount.

Now, then, to convince one's self that the sum of all these minute parasitic quantities are swallowed after being collected on the terrain of their development can reach a noteworthy toxic force, one needs to grasp clearly two conceptions only which have at length been acquired by science:

1. The parasitic moulds of Indian corn produce poisons which act powerfully on the nervous system.

2. The characteristic of these poisons is not to produce the phenomena of immunity, but, indeed, to hypersensitize the system to react to their repeated stimulus.

This true form of anaphylaxis, now admitted by investigators, susceptible of the most complete proof of the laboratory, was understood as an indication of the specific relation to the easy relapses of pellagra, and is also confirmed, though in an indirect way, by the same recent investigations of Volpino and his collaborators.

The pellagrin who comes forth from the sanitary eating houses [*locande sanitarie*] as cured is always the most common candidate for the disease, into which he relapses repeatedly and very easily. When once the tendency has developed the symptoms break out afresh every year with progressive aggravation of the process up to the point where there is no relief. And as the alcoholist acquires gradually such a susceptibility to alcohol as not to be able to resist the disastrous effects even of small quantities of wine and liquor, so we have said and still say, until the contrary is proved, the pellagrin gradually hypersensitizes himself up to the point of feeling the slightest toxic tendency, especially of those poisons which can not be guarded against in the trade in cereals and which (to repeat what we have just said) are amply provided for this toxic effect, both by the great quantity of polenta which the individual eats and by the very great facility with which corn meal can be spoiled. And thus arise pellagrous psychoses, severe conditions of amentia (typhoid pellagra), and spastic paralysis; all this would represent for

toxico-zeism that which delirium tremens does for alcoholism. And the analogy goes still further; alcohol causes symptoms of cutaneous eruptions, just like a *pelle agra* (rough skin). Again, if there is here a hereditary pellagra, there is also there a hereditary stigma in the children of alcoholists, with a specific organic degeneration; the difference in the two poisons is able to make a different appearance in the two cases, but the theoretic strength of the analogy is real and it is significant for possible scientific and practical deductions.

If a fermentative process of sugar conduces to products whose abuse causes phenomena similar to pellagra, this encourages one to derive pellagra also from other fermentative processes of the hydrates of carbon—processes which we have demonstrated to be generators of toxins under conditions already explained.

Single points of uncertainty have existed, and still exist; we, ourselves, have brought them up and still do so; but these can be differentiated in distinct relief by their different natures; thus if it is undeniable that there is pellagra without corn, it is simply the case that the hyphomycetes invade other foods in common use. If great numbers who are dependent upon an extensive diet of spoiled corn, are free from pellagra, one must simply remember that not all the hyphomycetes are toxic, nor are the toxic ones of the same degree of toxicity everywhere, for they can have very noteworthy differences, in this respect, owing merely to the varying temperature in which they exist; and then there is also the variable individual receptivity towards the poisons which has been well proven by experience (Paladino); and there is likewise the consideration of alcohols specifically toxic and spread through the commerce of some countries. And finally, there is undeniably a diversity in the clinical forms of pellagra; then, we repeat, it can very well be admitted that, just as in so many other diseases, also here one and the same term embraces morbid entities which will unfold themselves later as having different relations to etiology.

Furthermore, to the one claiming that the facts collected in the practical field are all explained and clear, we would say that scientific investigation is often not able to do more than touch on the prominent features, and these are roughly illustrated in the artificial work of the laboratories. The rest ought to be deduced and brought to the standard of truth by reasoning; otherwise there is not an

endemic disease free from doubt and obscurity. Do they not discuss every day the enigmas of cholera, though its specific germ is in our full possession?

In conclusion, *we are far from sustaining the proposition that our undertaking belongs to the class of things which we are accustomed to call simple truth; much still depends on indications, but the indications in this case are sufficient to keep us from giving up faith in the present law for the prophylaxis against pellagra.*

Have the other theories which threaten this one with destruction a better foundation? Let us see in a brief examination.

The theory, which, by reason of the mass of experiments and positive findings accessible to every investigator, deserves to be placed in most prominent view, is that of Tizzoni. He supports the view of the infectious nature of pellagra and indicates its agent in the germ which he already calls "streptobacillus pellagræ."

This theory has been proclaimed now for fourteen years and lately has advanced so far as to promise even a serological diagnosis and an antipellagrous vaccination.

We should be glad if the views of Tizzoni would prevail definitely, so much the more as with it the carrier of the pellagrogenous infection would always be spoiled corn; so, on the one hand the law would preserve its own specific value (perhaps would finally exaggerate it too much), and on the other, valuable measures would be taken for the better identification of the disease and for preventing it. It is right, however, for one to recognize the fact that, though the fruit of severe, patient, admirable labor, the work of Tizzoni still lacks the proof and support to entitle it to be received as the basis of practical application. The credit due for acquiring these would be gained when the well known fundamental canons of Koch shall have been satisfied: *"Finding the germ in all the cases of the selfsame disease; its isolation in pure culture from the infected organism; reproduction of the disease by means of the pure cultures."*

To forestall the necessity of interpreting them today with much greater rigor and with special discernment, we may simply say that it is still doubtful if such canons find in the acquired facts that strict accord which one exacts before being fully convinced. Some investigator now finds the discovery of the specific germ well confirmed; but presently others find that the test had altogether negative results, even following the precise technique suggested by

Tizzoni (Lavinder); nevertheless, the experimental test made recently in the asylum of Mombello gives entire satisfaction not only for negative findings in tests of pellagrous individuals, but also for positive findings in case of a person affected by another disease. If such observations should be repeated they would lead to a great diminution of the specific value claimed for the "streptobacillus pellagræ."

Furthermore, the morphological, biological and cultural characteristics of the said germ do not observe the limitations which we are accustomed to fix for specific bacillary unity; sometimes one finds a true streptobacillus, another time a streptococcus or a diplococcus or, again, a staphylococcus comes into view, and, as the morphology and cultural aspect vary, doubt is cast upon the identity of the so-called original stock; and so much the more as not rarely these latter appear very scattered and mixed with organisms of a decidedly different nature. And if the signification of similar metamorphoses ought to be understood according to the various clinical forms of pellagra, still some greater light, some greater contribution, is indispensable to render secure and constant the bacteriological data in agreement with single clinical entities.

Also the reproduction of the disease in animals leaves us perplexed to decide whether the picture already formed is truly reproduced from the specific point of view; the necessity of large doses and of repeated inoculation in the same animal in order to induce a morbid process which can lead to death after a long time (a year) without a trace of the specific germ being found there renders us uncertain in judging it.

Nor do the serological tests argue more strongly for the asserted value of the micro-organism discovered by Tizzoni; up to the present a complete study of agglutination, with experiments anxiously awaited, has been wanting, especially in quantitative respects, because the qualitative tests are far from inducing the conviction of a specificity.

Finally, beside the above mentioned scarcity of discoveries of micro-organisms even in cases of very severe pellagra, further impressions are made in opposition: *The fact that there are no positive data as to the so-called bacterial focus,* which, however, are never wanting in other infections of toxogenic character; *the difficulties of guarding the very delicate technique from error; the doubt*

that common hemolytic germs of the species described emigrate in the blood because of an organic damage, for establishing, in this last regard, a true guaranty one would admit that it does not suffice to exclude from examination the sick with bedsores; also simple lesions of the mucosa intestinalis, obvious in one who sometimes suffers from digestive disturbances, can constitute infection atria for such invasions of common micro-organisms.

However, in the present state of the question, he who should express, as to this point, a conscientious opinion would find himself in the midst of serious opposition. We certainly do not intend here to substitute for the criterion of him who for almost fifteen years dedicates his energies and the authority of his name to the new theory. *Charged with rendering an opinion, we feel rather the duty or necessity of an objective demonstration.* If one demands here conviction, it is right that we be able to have at our disposal criteria free from ambiguity. And we are so much the more led to entertain reservations, because there have already been too many micro-organisms, which, though borne with clear conscience to the altars of science even by illustrious bacteriologists as the certain causes of such infectious diseases, had still to fall to the ground after more mature criticism.

We prophesy that this will not be the fate of the "streptobacillus pellagræ," but predict that over this question profound investigations and controls on a vast scale are going to be undertaken and we shall be glad, indeed, if we shall be able to subscribe to a corollary which in the end, by bringing a new contribution to the truth, would save the present law on pellagra and illuminate its spirit.

Much more hypothetical are the theories of Sambon and Alessandrini, who regard more developed parasites as the cause of pellagra.

Too much has already been said and written for the purpose of establishing these hypotheses in comparison with what has been expressed to define the position which, for the present, we ought to occupy in regard to such views. We have stood a long time waiting and we take a lively interest in the investigation of these positive elements, which, if established, would put an end to all controversy and place the problem upon a firm basis.

These elements are obviously deduced from the history of other diseases with which pellagra ought to be called analogous, if it were really an infection transmissible by the bite of insects, or by

larger parasites inhabiting polluted drinking water. In the first case we have the example of malaria; in the second, that of various helminthiases, of which some are known in all their details. We know the three classic fundamental features which ran through the problem of malaria before a satisfactory solution was reached: "*The discovery of the hematozoa—demonstration of the endogenous cycle (agamie) in man—demonstration of the exogenous (sexual) cycle in an intermediary host;*" the third feature is to assert the crucial experiment, the reproduction of the infection by means of the biting host in organisms certainly sound.

We know analogous cases, *e. g.*, the natural history of the anchylostomiases, of some filaria, and, not to trespass into neighboring fields, of trichinæ and of teniæ.

So then, before being converted to the views of Sambon or of Alessandrini, shall we wait to see what light may be thrown on the claims of similar parasitic classes? Very far from such an intention, we are satisfied with a single one of the convincing final points, *e. g.*, to know, at least, the responsible parasite or, indeed, to have unmistakable proof of infection which would demonstrate their existence and also their generic peculiarities. These points of encouragement are wanting, and everything up to the present moment bases itself on epidemiological findings, on topographical distribution of insects, a method of procedure in which the difficulty of sticking to the objective facts is demonstrated by the very circumstance that the study of the nosographic surroundings themselves gives admission to two entirely discordant theories concerning the pathogenetic mechanism; *the one is for still water; the other for running water; by one the disease is acquired through drinking water; by the other it is acquired by inoculation.*

There is no obstacle, either in this respect or in that; tomorrow one learns what he is ignorant of today; the same accuracy and impartiality with which Alessandrini proceeds in the practical investigation of the endemy in its relation to drinking water, could help, in a praiseworthy manner, the cause of future victory and, in every sense, whatever may spring from an accurate, faithful and encouraging labor. A helpful contribution is always to be welcomed.

To us, at present, it is a matter of anxiety only to prevent any one from coming to a conclusion too soon, or, what is still worse,

acting as if a conclusion had already been reached in antagonism to what the law prescribes.

Although the theories of Sambon and Alessandrini are the most plausible of the sudden divergences from the original principles, up to the present professed by the majority, still there are several others which have helped to throw those around them in confusion and destroy the faith of the zealous. The theory of simple maidism, unfitness and insufficiency of nourishment and the so-called photodynamic theory, deserve a word or two.

The first was so thoroughly discussed at the last congress, by Asudenino especially, as to render it superfluous to treat it here in detail; it is indisputable that experimental animals react against the exclusive use of even sound corn, as against an unfit diet, and that organic damage follows it; to which, in certain limits, one can attribute a feature of specificity. Is this pellagra? We deny it; we recognize, however, the necessity of giving to the fact its due importance, to admit the possibility of morbid forms there, which, through these symptoms, approach pellagra and constitute a part of the morbid entity going under that name, and finally take account of all this with practical prudence. The theory of *mere alimentary insufficiency*, harking back to the oldest conception, perhaps, of all (Lussana), takes refuge in a fitting experimental appreciation, while on the other hand it opposes the admission of a connection of specificity with a cause, which ought to be able to be found also outside of maize alimentation. Among technicians it is now very difficult for such a conception to find credence; and indeed, for the sake of warning, to show the disastrous effects which can be produced in the practical field by a proclaimed division among the etiological views. We recall the fact that a recent investigation, made in one of the provinces the most infected with pellagra, had the following result: Of seventy-two physicians who were questioned, sixteen declared themselves for the toxic theory, six for the theories of infection, and all the others (35) for the theory of alimentary insufficiency; a disease indubitably extremely specific *in its true type*, ascribed, as if by a plebiscite, to one of the most commonplace causes!

The photodynamic theory is an ingenious union of solar influence with maidic condition; the food maize, which would be harmless in itself, would become pellagrogenous with amboceptors alone!

Raubitschek, as is well known, starting out from the fact that the pellagrous erythema is, in general, limited to the parts exposed and hence subject to the action of the rays of the sun, puts forth the hypothesis that under the influence of maize diet, in the parts of the body exposed to the action of the sun, a noxious substance is developed which not only induces alterations in the exposed parts, but does injury to all the system. For this he institutes a relation between maize diet, solar rays and pellagra.

He experimented upon white and gray rats. Some cages were exposed daily to the direct rays of the sun, others were protected against the light, others still were kept in perfectly dark surroundings. The animals were nourished partly with spoiled maize, partly with sound maize and others with wheat and other normal substances.

According to the author the animals of white color and exposed to the light, died outright or gradually wasted away before the gray or white ones, which were kept away from the light.

Nor do the speculators stop here, for, rendered bold by the apparent failure of science, they advance the strangest hypotheses and finally come to the point of explaining pellagra as simply the effect of anchylostomiasis.

What is to be said of the other hypotheses not sustained by experiments nor by epidemiological data, which appear in swarms these latter days?

For example, that of Ravitch-Eisenman-Prudy (The Lancet, July, 1912), which holds the view that pellagra is originally a disease of certain migratory species of blackbirds and is transmitted to man by common flies! In every period some one is found who is carried away with the fancy of investigating strange things which he thinks may be the cause of the disease, and they justify Lombroso when he terms them the vagary-hunters of pellagra.

We will not take time here to describe the sad moral and material effects of such vagaries; we urge that their very number is only a stimulus to follow the way today best known, and we conclude by placing in view one consideration which argues for complete harmony of spirit and unity of strength. These doctrinal absurdities, these scientific discrepancies encourage the speculators who have already preached as gospel what, in reality, remains always an obscure hypothesis; these persons, though not able to lay hold of

a single certain proof, proclaim that there is no connection between spoiled corn and pellagra, supporting the new theorists and aiming at the abolition of the law; the mildest of them claim, at least, rather large concessions in reference to the trade in spoiled corn meal, in damaged corn grain and that liable to damage; and here and there is a succession of protests, a coalition of industrial leaders, who, thinking themselves injured in the right of not going very carefully into the matter of mere hygiene, proclaim with great boldness that scientific failure ought not to express also business failure, as if it were business failure not to be able to sell damaged Indian corn!

However each one may think, all ought to cry out in a single voice against these pernicious tendencies; let us await still faithfully for more light in the future and let us give it what help we can; let us all enlarge the scope of science and aid more deeply and more calmly its researches and its investigations of the etiological problem, eliminating those destructive critics whose only aim is an apparent desire to produce discord. In the meantime, let us take care not to tear down before we know what it would be best to build up. And, in this regard, the Fifth Italian Pellagra Congress and the American National Association for the Study of Pellagra at its second session would be wanting in their duty if they do not advise and urge unity and seriousness of purpose.

Rome, Milan, August, 1912.

A REVIEW OF RECENT HYPOTHESES UPON THE ETIOLOGY OF PELLAGRA.[1]

By DR. VICTOR BABES, Professor of Pathological Anatomy and Director of the Pathological Institute, Bucharest, Roumania.

Since 1907 the condition of the Roumanian peasant has been improved. In spite of economic and sanitary amelioration, however, the number of pellagrins in Roumania has increased, being today about 80,000. The total population of Roumania is 7,600,000.

As a rule the cases are not severe. Most of them are so light that they do not come to the hospital. They continue at work and recover. Relapses are frequent, though, and it is only after repeated attacks that doctors see them and they are put in hospitals. Still the number of severe cases is not large. Therefore the total number of pellagrins does not mean an equal number of degenerates, lunatics and broken down farmers. Nevertheless, pellagra is a calamity for Roumania.

In spite of the rich literature on pellagra, scarcely so important a malady exists about which we are so badly oriented. One thing only seems to be established about its etiology: that it belongs to the diseases of poverty, of insufficient alimentation, and notably that it is in intimate relation with nutrition by maize of bad quality. But apart from the distress resulting from economic and sanitary defects, it is necessary to reserve a considerable place in the predisposing causes of pellagra for congenital maladies, both endemic and infectious, which exist in pellagrous regions, such as idiocy, endemic goitre, malaria, syphilis, etc. Thus among 250[2] pellagrins examined closely, there were found:

Presenting signs of congenital weakness....	30
Cretins	26
Goitrous	32
Alcoholics	112
Malarials	120
Syphilitics	90
	410[2]

[1]This paper has appeared in Atti del 1° Congresso Internazionale dei Potologi. Torino, 1912, p. 122, and is contributed by Professor Babes to these transactions.
[2]These numbers are printed as they are given in the original.

Among these several presented an association of two or more of these predisposing affections. The majority of pellagrins belong to the most needy class of the population, and in many cases pellagra has made its appearance in individuals who have met with great losses or been stricken with misfortune, compromising their economic condition. From this it is clear that predisposition plays an important role in pellagra.

If the economic and sanitary reforms of the latter years have not, up to the present time, produced the hoped for results, the cause of it is, without doubt, that it necessarily takes much time for these reforms to reach the hearths of the poor. Even in Lombardy, where the lot of the peasant is better than that of the Roumanian, pellagra is yet widespread.

To combat the disease successfully, therefore, it is necessary to look for other and more feasible means based upon its etiology. With this in view, it is necessary to take account, in the first place, of all the serious work which has established the maidic origin of pellagra, notably, that pellagra, as a malady of the people, exists only in the countries where the food supply is chiefly corn, and especially of the work of those who have proven the disastrous effect of nourishment with spoiled corn. I can add that in 1906, following a bad crop, the government was forced to import foreign corn, and of bad quality, when at once pellagra increased in a disquieting manner. From my numerous investigations, the same fact is proven, namely, that the majority of pellagrins are among the poor and that they have eaten spoiled corn; finally our chemical researches (A. Babes) have shown that it is especially from spoiled corn that toxic substances may be extracted. Notable among these oils poisonous to animals, which fall ill with symptoms having a certain analogy with those of pellagra. As all corn contains a certain quantity of spoiled grains, one finds in it, without doubt in every case, toxic substances, though possibly in small quantity, and these may prove especially pathogenic for predisposed persons. Our experiments, confirmed by Italian authors (Antonini), which show that one can, to a certain extent, combat in animals the toxic effect of these products by the injection of serum from old pellagrins, plead likewise for this conception.

It is necessary, however, to note that lately several writers have given expression to the opinion that there is no relation between

spoiled corn and pellagra and that the malady can be produced just as well by nourishment with *good* maize, and still others deny absolutely the maidic origin of pellagra. Among these latter it is necessary to mention Sambon, who, after having visited several pellagrous regions, affirms that pellagra has nothing to do with alimentation with corn, but that it is produced by some species of *Simulium*. He declares that it is the geographic distribution of these little insects and not nourishment by maize, upon which the distribution of pellagra depends.

However, *Simulium reptans* and other species of these small insects are very widely spread throughout humid regions, irrigated by many watercourses, of all parts of Europe, and notably in the countries where there exist neither corn culture nor pellagra. These flies appear in the spring much later than the eruption of pellagra. They fly in great swarms after having passed the larval state in running water, and especially on reeds. These insects often bite men and animals, especially on the face, producing only passing irritation, with the exception of the *Simulium columbacense*, whose multiple bites cause in animals swellings of the respiratory mucosa, followed often some hours after the bites, by death of the animals. I myself and Sambon have found *Simulia* in Roumania, also *Simulia* both in the regions where pellagra existed and also where it did not exist, but so far neither Sambon nor I have found any relation between the insect and corn. It seems to me that this fact by itself suffices for discarding the theory of Sambon But one may add still other reasons:

1. It is not sufficient to find in pellagrous regions any insect whatever, biting and living upon blood, to be able to affirm, based upon this fact alone, its etiologic relationship with pellagra; especially as this insect is found also widespread and in large numbers in non-pellagrous regions; the mere presence of *Simulia* in pellagrous regions does not constitute proof of its relationship with pellagra.

2. Since pellagra, as a common malady, is indubitably allied to maize, it is necessary to find some relationship between the insect producing or transmitting pellagra and corn.

3. It is necessary to prove that pellagra exists as a common malady in regions where the population does not eat corn.

4. It is necessary to prove that in regions where there are no *Simulia* there exists also no pellagra and that in these regions there are no other conditions which prevent the appearance of the malady.

5. It is necessary to be able to produce pellagra experimentally through the mediation of *Simulia*.

6. It would be necessary to establish some relationship of specificity between pellagra and the insect.

7. It would be necessary to find a parasite in the bodies of pellagrins and the same parasite in *Simulia*, to be able to affirm with all certitude an etiologic relationship between the Simulia and pellagra.

8. It would be necessary to establish a relationship between the epoch of the appearance of Simulia and the appearance of pellagra.

9. It would be necessary to find out whether, in eliminating *Simulia* in a pellagrous region, pellagra disappears.

Only an intermediary insect or a parasite fulfilling many of these conditions can be recognized as playing an essential role in the etiology of the malady.

It seems to me unfortunate that the role of certain moulds or microbes in the etiology of the malady, claimed by certain authors, is not better established. However, I have tried to convince myself by my own researches of the claimed relationship. At first I cultivated on various media certain forms of microbes and moulds obtained, on the one hand from pellagrous maize (corn and meal from spoiled corn from the dwellings of pellagrins and serving as their food), and on the other hand from the bodies (skin, mucous membranes and excretions) of pellagrins, and examined whether there exists a relationship of specificity between these micro-organisms and pellagra. In like manner I procured a series of micro-organisms, bacillus maidis, aspergilli, penicillia, and mucor, of which different authors have affirmed that they have a relationship with pellagra and produce in animals under certain conditions lesions analagous to those of pellagra.

The result of our investigations made in collaboration with Busila upon these organisms, as well as our studies on the relationship of different chemical substances extracted from spoiled corn obtained from pellagrous territory is as follows: It is especially in employing the methods of agglutination and of deviation of complement that we should find out whether certain organisms from the bodies of

pellagrins or of spoiled corn or of certain substances derived from corn, reputed to be in relationship of cause and effect with this malady, give with the serum of pellagrins a specific reaction. To this end we at first attempted the agglutination of the following organisms with the serum of six pellagrins presenting different forms, acute and chronic, of the malady.

1. Cultures of organisms derived from the skin and intestines of pellagrins.

2. Bacilli belonging to the typhoid-colon group derived from the organs, fecal matter, or urine of pellagrous individuals or the bodies of those dead from pellagra—none of these have been agglutinated by the serum of the six pellagrins.

3. Cultures of organisms taken from corn more or less altered (cocci, bacilli, streptothrix and a microbe analagous to the bacillus maidis), but none of these have been agglutinated by the serum of our pellagrins.

4. Finally we obtained from spoiled corn serving as food of pellagrins, some moulds corresponding to the moulds described by Ceni and others, aspergillus fumigatus, pathogenic aspergilli and penicillia of other production cultivated summer and winter. All these micro-organisms tested by the serum of twelve pellagrins or old pellagrins, gave a negative result. The cultures of moulds obtained by Sion from spoiled corn, tested also by our serum of pellagrins and old pellagrins, remained likewise without effect. Certain microbes of the typhoid-colon group isolated from diarrhœal dejections of pellagrins showed a feeble agglutination, not exceeding the agglutination obtained by normal serum (1:20 for example). Another series of experiments has been undertaken to try to obtain a specific system formed on the one hand by an antigen taken from the bodies of pellagrins or from altered corn, and on the other hand by an antibody, namely, the serum of pellagrins.

1. The microbes and moulds mentioned have been employed as antibodies sometimes in emulsion, sometimes in aqueous or ethereal extract, sometimes in solution in antiformin, neutralized by sulphuric acid, while the serum of twenty-six pellagrins obtained from acute and chronic forms or old pellagrins has served as antibodies.

2. We have also tried as antigens the urine and the dejections of pellagrins as well as the altered skin of pellagrous cadavers.

3. The chemist of our institute, A. Babes, has placed at our disposal extracts, ethereal, alcoholic, and aqueous, from spoiled corn. Among these extracts some are soluble, others insoluble in petroleum ether. These substances, which are in part toxic for laboratory animals, and produce an irritation of the skin, falling of the hair, marasmus, convulsions, or paralysis and death, have been tried also as antigens. As antigens, also, we have used, on the one hand, colon bacilli, two aspergilli, pathogenic penicillium glaucum, their extract, lecithin and the extract of the heart of a guinea pig, on the other hand, as antibodies, normal and syphilitic serum.

In none of these experiments have we been able to establish the formation of an amboceptor, either for the pellagrous serum or for the control serums. A single time a mould cultivated from pellagrogenous mould yielded this spring a feeble deviation of complement, while the experiments made later, after repeated attempts, remained negative. We finally tried two kinds of oil, red, toxic, extracted from spoiled corn, and an oil from maize not spoiled, with the same negative results.

It appears, then, from these researches that the micro-organisms and the extracts experimented with up to the present show: The micro-organisms isolated from the bodies of pellagrins, emulsions, solutions or extracts of these microbes derived from pellagrous bodies, the characteristic diarrhœal dejections of pellagrins, the commonest micro-organisms, the pathogenic micro-organisms, aspergilli, penicillia, and mucor, which we have found in spoiled corn taken from the dwellings of pellagrins, do not show specific relationship with the blood serum of patients.

In face of these rather discouraging researches, the publications of Raubitschek, who supposes that pellagra is only a photodynamic malady, have been favorably received. This author fed some white mice on ordinary corn, then he exposed them to the sun and observed that these mice developed a malady analogous to pellagra. The hair fell, the animals weakened and died; while the evidence of the same writer is that the gray mice treated in the same manner remained quite well. In like manner alcoholic extracts of good corn or bad, produced the same effects on white mice. It is true that other grains rich in oil produce on white mice the same effect, and the oil extracted from corn, mixed with flour, would also yield these symptoms in white rats exposed to the sun. Raubitschek

concludes from his researches that corn contains an oil which becomes activated by the light of the sun, and that pellagra is consequently a photodynamic affection. I am not able to accept this point of view. For we have succeeded in producing symptoms like pellagra in white or colored rabbits, in guinea pigs, in dogs, again in chickens which have not been exposed to the solar rays. Furthermore, pellagra does not always begin in spring and in people exposed to the sun, but most of the time the eruption develops in persons already ill, who in part do not work in the fields. I have even found that often the first manifestations, which are generally of a nervous or intestinal nature, begin generally in winter or at the commencement of spring, before the peasant has gone to the fields. Furthermore, children whose skin is more sensitive than that of adults, rarely fall ill, and, on the other hand, gypsies and negroes are not exempt from the malady. Finally, most peasants fed almost exclusively on corn and exposed to the sun quite as much as the pellagrous, do not develop pellagra.

We have known for a long time that the rays of the sun play a certain role in pellagra, but they are not the first or chief cause.

We do not know, furthermore, whether circumstances other than the burnings of the sun and which develop their force when the parts not covered are exposed to the free air, do not co-operate to irritate the predisposed skin.

There are also other maladies which attack especially uncovered parts and those exposed to the sun, without this peculiarity being explained by a photodynamic action of the sun—leprosy, for instance.

We must suppose, then, that besides maidic nourishment, there is yet something necessary in order that, at a given moment, the very same burning of the sun which in the case of the selfsame man or in the case of other men living under the same conditions has caused no sickness, may produce now the pellagrous erythema. That which has developed itself before is precisely a weakness and a disposition due to spoiled corn. If we make serious inquiry among pellagrins we find in many cases that the patients recall quite clearly that during the winter, before going to the fields, they were already sick and especially very weak and neurasthenic, that they could with difficulty go about, and that they had pains in the loins, headaches, vertigo, a sensation of smarting, pyrosis, diarrhœa, etc.

In short, if the toxic substance of pellagra does produce itself only under the influenec of the burning of the sun, one cannot explain the aggravation of the pellagra in the case of pellagrins who neither longer go to the fields nor expose themselves to the rays of the sun. In the case of these sick persons the poison should no longer produce itself and they ought then to get well rapidly.

In taking, with care, the anamnesis of fifty cases of pellagra this is what I found in each:

1. Pellagra began at the beginning of March, during convalescence from typhoid fever.

2. Began in spring with erythema.

3. Began in January with contractions of the pharynx and the sensation of burning in the esophagus, then erythema followed.

4. Began in spring with malaria and nervous symptoms, then erythema appeared.

5. Began in April with great weakness, vertigo, then erythema and diarrhœa.

6. Began before appearance of erythema with loss of appetite, pyrosis, headache, asthenia, vertigo.

7. In a girl very anemic, who had scurvy and purpura on the neck, spring brought out the erythema and edema.

8. Upon a patient living in a region where malaria and scrofula are endemic and after his recovery from typhoid fever, erythema appeared in the spring.

9. Diarrhœa followed in the spring by painful erythema of hands and feet.

10. The malady began by headaches, diarrhœa, the erythema did not occur until the second year.

11. In winter, after an operation for hernia, diarrhœa, neuralgia, and weakness set in, and in spring erythema began.

12. The malady began with pains in the head, vertigo, heart trouble, pyrosis, the erythema appeared the second year.

13. The trouble began with a cough, burning in the stomach, pyrosis, then a bullous erythema appeared even in the mouth.

14. Began with malaria, profound anemia, then in the spring, erythema.

15. The patient has suffered from malaria and typhoid fever; the pellagra began in winter by neuralgia, pyrosis, diarrhœa; in spring erythema appeared.

16. The malady began in winter with weakness, vertigo, hemoptysis, then, in spring, erythema.

17. Began in spring by erythema.

18. The trouble began in summer by nervous irritability of the skin, hallucinations, neurasthenia, the following spring erythema appeared.

19. In winter, pain in flanks, heart trouble, pyrosis, weakness, then, in spring, erythema began.

20. Malaria, commencing with migraine and periodical swelling of the right side of the head. At end of six months erythema.

21. Cretin.

22. Goitrous cretin.

23. Declares that the next day after eating soup made from spoiled corn erythema and pyrosis began (?).

24. Began in spring with erythema.

25. After an operation (lithotomy) erythema with mental confusion began.

26. Just before Easter, weakness, disinclination for work, tingling sensation in the hands and feet. At the end of a week, erythema.

27. The malady began with headaches, fainting, pains in the hands and feet, then the erythema appeared.

28. Diarrhœa continued during winter, with gastralgia and pyrosis. Erythema began in spring.

29. In winter, up to February, a pulmonary trouble with difficulty in respiration, cough, fever, cephalalgia, in March erythema, painful and with fissures.

30. Began in spring with erythema.

31. As 30.

32. Began in spring with headache, weakness, depression, vertigo, pain all over the body; at the end of a month erythema began.

33. As 30—on the breast.

34. Began in the spring with erythema.

35. As 30.

36. As 30.

37. In summer the patient had indigestion, stomach trouble, vomiting, diarrhœa, fever, dysentery, then the erythema appeared.

38. Commenced at beginning of spring—erythema.

39. Fever, enteralgia, then erythema in spring.

40. Began in March with diarrhœa, erythema appeared in April.

41. Tuberculosis, miscarriage with excessive hemorrhages, weakness in winter, erythema in spring.

42. Tuberculosis, hemoptysis, followed by erythema.

43. In spring headache, weakness, then erythema.

44. Began in spring with diarrhœa, at end of two weeks erythema.

45. Began as erythema and diarrhœa.

46. Alcoholic, fell ill in winter with weakness, lumbar pains, fainting; erythema appeared in spring.

47. Began in April with erythema.

48. Began in autumn with headaches, fever, enteralgia, dysentery towards February, at end of four months erythema appeared.

49. Began at first of spring by erythema.

50. Malarious syphilitic, depressed, alcoholic, beginning of pellagra with erythema.

Thus, then, in only twelve cases of fifty carefully examined, the illness began at the commencement of spring by erythema of the parts exposed to the sun, the thirty-eight other cases could not be explained according to the hypothesis of Raubitschek, who supposes that it is only the heat of the sun which produces on the parts of the skin exposed to the sun a toxic decomposition of the fatty element of corn, which determines, as the first manifestation, the erythema of pellagra.

The hypothesis of Raubitschek is not, then, tenable, most pellagrins having already been sick at the moment when the toxicodynamic effect of the sun was produced; this effect is not produced because the individuals are fed with corn, but because they are already ill when they are exposed to the sun.

In applying the points of this investigation to the white rat cases of Raubitschek, one can say the white mice fed on corn represent individuals already pellagrous, who, exposed to the sun, develop toxic symptoms, while the gray mice fed on corn represent individuals who are not pellagrous. Yet the experiments of Raubitschek tend to explain simply one of the symptoms of the malady which is produced in individuals already pellagrous, but they do not prove at all that this solar action is the cause of pellagra. From the moment that the hypothesis of Raubitschek cannot be sustained in absolute form, we cease to admit any longer his conclusions as to what, even whether sound corn, produces pellagra. Even the

experiments on which he bases the hypothesis, being partly in contradiction with my experiments, ought to be well controlled and extended. Raubitschek, himself, admits that white mice being much exposed to the sun contract almost the same malady when nourished with other cereals containing much oil. In other words, white mice seem to be very sensitive to many vegetable oils. Thus, then, while in the domain of the etiology of pellagra there has been made scarcely any progress, for all the efforts to solve the cause of the malady cannot be considered as successful, I believe we have obtained certain points of success in the treatment of pellagra.

In 1907 and 1908 I had occasion to address the Roumanian Academy regarding our efforts to cure pellagra with injections of atoxyl. Our results obtained in collaboration with Vasiliu and Gheorghiu, of Roman, have been also published in the Berliner Med. Woch. in 1907 and 1908. Indeed, having followed this treatment with Dr. Vasiliu, chief physician of the department of Roman, which is most ravaged by pellagra, and Dr. Gheorghiu, interne of the pellagra hospital of Pancesti-Dragomiresti, I am convinced more and more of the efficacy of this treatment. Likewise, the experiments made with this substance in the hospitals of Bucharest, of Maicanesti (Dr. Campeanu), of Dorohoi (Dr. Apostoleanu), of Dalj (Dr. Draghesco), etc., have yielded good, often even excellent results. I have now the results obtained in cases of 124 persons treated with atoxyl and with other arsenical salts and am justified in drawing the conclusion that atoxyl, applied in a careful manner and individualized, gives excellent results. As this substance is demonstrated as efficacious, especially in certain infectious maladies of a parasitic nature, produced by protozoa, we may suppose that pellagra, the cause of which has escaped our observations, belongs to this same group of maladies. I can affirm that this treatment associated with rational feeding renders the patients in one or two weeks capable of work. I have, therefore, proposed to our government to practice this treatment on a large scale.

Résumé: We have shown that not one of the micro-organisms or moulds found in spoiled corn or in the bodies of pellagrins, nor even the chemical product extracted from corn, show with the serum of pellagrins either agglutination, or the fixation of complement. Likewise, up to the present, none have given proof, and I have not been able to convince myself of an essential role which

is said to exist between the Simuliidæ and pellagra; finally, the hypothesis of Raubitschek, according to which pellagra would only be a photodynamic malady produced by corn, spoiled or not, is not tenable. It is true that the rays of the sun have a pathogenic action upon pellagrins, but, in the majority of cases, the individuals suffering from solar action have previously been pellagrous. It is necessary, on the contrary, to remember that the hypothesis, according to which it is especially alimentation by corn, more or less spoiled, which produces pellagra, remains supported by the best evidence. It is necessary to add that a certain morbid disposition created by poverty, by certain congenital predispositions or by certain diseases, is an essential condition for the development of the disease. Although the question is of a malady essentially toxic, one cannot exclude the possibility that an infectious parasitic element may intervene in its etiology. This last supposition finds a certain support in my encouraging results in the treatment of pellagrins by atoxyl.

There is still much uncertainty and obscurity about the etiology of the malady, and especially after the insufficiency of recent investigations has been established, the result of it all is a grand disorientation. The Italian commission for the study of pellagra, composed of savants of great competency, work with assiduity to dissipate this obscurity which hovers over the etiology of pellagra; however, it seems to me that it would be useful to associate with this commission an international committee, composed of pellagrologists of other countries, to undertake with one accord and according to a well determined plan, more extended researches in order to decide, in a positive manner, the etiology of pellagra.

In closing the discussion on his paper Professor Babes said: If in Roumania the latest economic and hygienic measures have not yet shown their effect, that proves nothing against their efficacy. Time is necessary for these measures to penetrate to the bedside of the poor of the population. I hope to be able to report in a few years more satisfactory results. I thank Prof. Dürck for the information on beri-beri. Immediately after the appearance of his fine work on beri-beri, we undertook new researches on the nervous system in pellagra, but I have already presented to the Congress of Naturalists at Munich, in 1899, a communication on the lesions of the nervous system involving also the brain and peripheral nerves

in pellagrins. These lesions resemble the lesions that one finds in certain cases of general paralysis. Volpino recalls that I am a partisan of the specificity of pellagra. However, while, in former researches, I have found that the serum of old pellagrins protects animais from the disastrous effects of certain maidic toxins, my new researches have not been able to disclose a specificity in the sense of agglutination and of fixation of complement. The researches of Volpino, while they can be explained by the great nervous sensibility of pellagrins, appear to indicate, at the same time, a relation between maize and pellagra.

Finally, I think I can close this interesting discussion by saying that we are all in accord on the maidic origin of the disease.

CONTRIBUTION TO THE STUDY OF ALIMENTARY BALANCE IN PELLAGRA.

By DR. JEAN NICOLAIDI, of Paris, France, and DR. UMBERTO GUILLO, of Udine, Italy.

INTRODUCTION.

In our first investigations in regard to the urinary excretion of pellagrins we found a marked diminution of the total nitrogen of the ash and phosphates; on the other hand, we were struck by the large proportion of ash in the feces.

The following year after repeating our studies on pellagrins in Italy, we arrived at the same conclusions: decrease in output of nitrogen and phosphorus in the urine appeared clearly in all the examinations undertaken. We also agree with Camurri when he says in his studies on "Metabolism in Pellagra" that "there can be in pellagra a *mineral diathesis,* as there is an *arthritic diathesis.*"

Convinced of the importance of these metabolic disturbances in pellagra, and more especially of the disturbances of mineral metabolism, we have sought to make a modest contribution to the study in question.

The results of the urinary analyses, as ordinarily carried out, are unsatisfactory. It is known how the results are modified under the influence of changes in diet. The sole method which we believe capable of giving precise results in the rigorous analysis of all the elements ingested, on the one hand, and the examination of the elements eliminated and the determination of the balance for each of the different elements adduced, on the other hand. This method practiced a long time in studying the various diseases of metabolism, has always yielded satisfactory results.

For the study of alimentary balance in pellagrins and nonpellagrins,, we have proceeded, with Dr. Grillo, in the following manner:

The individuals were kept for three days on their usual diet, the different kinds of food being exactly weighed, and the diet analyzed into its component parts. Then the urine and feces of the 24 hours of the third day were collected in receptacles containing an antiseptic to insure their preservation.

This part is certainly one of the most difficult and tedious of our labors and it exacts the greatest precision, for all the later results depend on the correctness of the figures first established. The arrangements necessary for this study have been ordered by Dr. Grillo, who, himself, conducted this part of our work with all care and precision.

Also, we may affirm that all of analyses made in our laboratory in collaboration with Mr. Paul Borden, carry guarantees of the most vigorous exactitude.

We undertook our investigations upon three groups of individuals—all three being subjected to the same diet, principally of corn:

Group I. Nonpellagrous individuals (normal).

Group II. Individuals formerly pellagrous.

Group III. Individuals with actual pellagra present.

The number of our observations is not large. The method used by us and the labor done will give an idea of the difficulties encountered up to the present in bringing to a successful conclusion the little which has been done.

This study will be prosecuted by us on a larger scale, and only after a certain number of observations will we be able to draw conclusions. We believe, however, that our first investigations enable us to present something of interest through the indications which we believe we can show on the nature of the disturbances of metabolism; without forming any conclusion and with all the reserve for the eventual modifications which our later researches may demand, we content ourselves for the present with reporting only the facts.

NONPELLAGROUS INDIVIDUAL (TABLE I).

Nourishment principally corn.

M—, Pietro, 34 years old, peasant, of M. (normal person).

The daily ration was 1988 grams (4 lbs. 6.12 oz.). The analysis in detail of each article of food shows, in the total of the chemical elements found, that the ration was sufficient in respect to its chemical components.

The comparison between the elements ingested and the elements eliminated gives, in the columns of balance, a positive result almost for all the elements. In the last column we have the calculated balance per cent. of each of the elements ingested in such a way that all the columns of the balance stand in a position for comparison.

In this case then of Table I all the elements show a gain. Indeed we find a gain of 20.12% of the nitrogen ingested, 28.74% of the salts, 10.29% of phosphoric acid, 59.16% of potash, 19.40% of soda, and 17.61% of chlorine. Only the balance of magnesium is deficient, with 25.60%, and that of calcium, with 16.90%.

The result is, then, that this normal, nonpellagrous individual is found to be in a perfect state with respect to alimentary balance, and that his system profits by each one of the ingested elements.

TABLE I.

Chemical Analysis of Foods Ingested.

	Weight, Gms.	Nitrogen, Gms.	Fats, Gms.	Carbohydrates, Gms.	Salts, Gms.	Phos. Acid, P^2O^5, Gms.	Magnesium, Mg O, Gms.	Calcium Ca O, Gms.	Potassium K^2O, Gms.	Sodium Na^2O, Gms.	Chlorine Cl, Gms.
Polenta	1100	6.941	5.412	332.200	13.885	2.750	0.737	0.594	2.013	1.928	2.200
Macaroni	100	1.380	1.260	71.550	0.711	0.237	0.058	0.104	0.146	0.087	0.099
Beans	100	3.280	1.670	46.360	3,590	0.870	0.272	0.177	1.759	0.120	0.137
Potato	30	0.289	0.067	5.493	0.393	0.054	0.013	0.012	0.206	0.002	0.002
Sausage	40	1.200	26.524	.....	3.024	0.176	0.007	0.033	0.136	1.192	1.360
Salad	80	0.400	0.544	3.224	2.280	0.154	0.081	0.204	0.474	0.062	0.070
Cheese	120	4.764	33.120	1.920	6.240	1.416	0.080	1.378	0.167	1.844	0.963
Olive Oil....	10	.....	9.995	.....	traces	.....	.....	.....	.....	.....	.....
Salt	8	.....	.....	.....	8.000	.....	.....	.....	.....	3.146	4.854
Wine c.c.....	400	.....	.....	.....	1.200	0.134	0.060	0.036	0.400	0.100	.....
Totals ..	1988	18.254	78.592	460.747	39.323	5.791	1.308	2.538	5.301	8.381	9.685

Comparison Between Ingestion and Elimination During a Period of 24 Hours.

	Ingested, Gms.	Eliminated.		Total Eliminated, Gms.	Balance.		Bal. Per Cent. of Materials Ingested.	
		Urine, Gms.	Feces, Gms.		Gain, Gms.	Loss, Gms.	Gain, Gms.	Loss, Gms.
Nitrogen	18.254	12.120	2.450	14.570	**3.674**	.....	**20.12**	.....
Fats	78.592	.....	8.100	8.100	**70.491**	.....	**89.68**	.....
Carbohydrates	460.747	.....	28.990	28.990	**431.757**	.....	**93.78**	.....
Salts	39.323	16.520	11.499	28.019	**11.304**	.....	**28.74**	.....
Phosph. Acid (P^2O^5)...	5.791	1.300	3.895	5.195	**0.596**	.....	**10.29**	.....
Magnesium (Mg O)....	1.308	0.132	1.511	1.643	.....	**0.335**	.....	**25.60**
Calcium (Ca O).....	2.538	0.082	2.885	2.967	.....	**0.429**	.....	**16.90**
Potassium (K^2O).....	5.301	1.273	0.892	2.165	**3.136**	.....	**59.16**	.....
Sodium (Na^2O).....	8.381	6.376	0.379	6.755	**1.626**	.....	**19.40**	.....
Chlorine (Cl)	9.685	7.302	0.677	7.979	**1.706**	.....	**17.61**	.....

INDIVIDUAL FORMERLY PELLAGROUS (TABLE II).

Nourishment principally of corn.

P—, Giulia, 43 years old, peasant woman of C—.

The weight of the daily ration was 2287 grams (5 lbs. 0.733 oz.). As in the preceding case, this ration is sufficient with respect to the various chemical component parts.

In this case we find some disturbance in the elimination of certain elements. In the balance we find a gain for nitrogen and for potash, and a loss for the other elements. Indeed, the gain is 5.28% for nitrogen introduced, and 1.5% for potash. The losses are 18.95% for the salt, 7.48% for phosphoric acid, 35.60% for magnesia, 39.55% for lime, 103.16% for soda, and 69.04% for chlorine.

But these losses are of little importance; they are insignificant in comparison with those which we have found in active pellagra.

TABLE II.

Chemical Analysis of Foods Ingested.

	Weight, Gms.	Nitrogen, Gms.	Fats, Gms.	Carbohydrates, Gms.	Salts, Gms.	Phos. Acid, P^2O^5, Gms.	Magnesium, MgO, Gms.	Calcium CaO, Gms.	Potassium K^2O, Gms.	Sodium Na^2O, Gms.	Chlorine Cl, Gms.
Polenta	1500	9.465	7.380	453.000	18.895	3.750	1.005	0.810	2.745	2.590	2.996
Milk	500	2.230	20.000	27.900	3.600	1.000	0.076	0.690	1.090	0.335	0.382
Bread	100	1.080	1.008	58.070	1.575	0.201	0.049	0.083	0.111	0.547	0.624
Rice	33	0.311	0.168	25.905	0.195	0.082	0.018	0.015	0.034	0.048	0.055
Macaroni ...	33	0.455	0.416	23.611	0.235	0.078	0.019	0.034	0.048	0.028	0.030
Beans	33	0.482	0.551	15.299	1.185	0.287	0.089	0.058	0.580	0.039	0.044
Sausage	20	0.500	13.262	.....	1.512	0.088	0.003	0.016	0.068	0.596	0.680
Salad	50	0.294	0.340	2.015	1.425	0.096	0.050	0.050	0.127	.....	.....
Olive Oil	10	.....	9.995	.....	traces	.....	.....	.....	.....	.....	.....
Salt	8	.....	.....	.....	8.000	.....	.....	.....	.....	.....	.....
Totals ..	2287	14.877	53.120	605.800	36.622	5.582	1.309	1.833	4.972	7.367	9.709

Comparison Between Ingestion and Elimination During a Period of 24 Hours.

	Ingested, Gms.	Eliminated.		Total Eliminated, Gms.	Balance.		Bal. Per Cent. of Materials Ingested.	
		Urine, Gms.	Feces, Gms.		Gain, Gms.	Loss, Gms.	Gain, Gms.	Loss, Gms.
Nitrogen	14.877	11.200	2.890	14.090	**0.787**	.....	**5.28**	.....
Fats	53.120	.....	16.090	16.090	**37.030**	.....	**69.71**	.....
Carbohydrates	605.800	.....	33.710	33.710	**572.090**	.....	**94.43**	.....
Salts	36.622	31.110	12.110	43.220	.....	**6.598**	.....	**18.05**
Phosph. Acid ($P^2 O^5$)	5.852	1.220	4.780	6.000	.....	**0.418**	.....	**7.48**
Magnesium (Mg O)	1.309	1.155	1.620	1.775	.....	**0.466**	.....	**35.60**
Calcium (Ca O)	1.833	0.068	2.490	2.558	.....	**0.725**	.....	**39.55**
Potasium (K^2 O)	4.972	2.363	2.534	4.897	**0.075**	.....	**1.50**	.....
Sodium (Na^2 O)	7.367	14.650	0.316	14.966	.....	**7.599**	.....	**103.16**
Chlorine (Cl)	9.709	16.000	0.412	16.412	.....	**6.703**	.....	**69.04**

INDIVIDUALS WITH ACTIVE PELLAGRA (TABLE III).

Nourishment principally of corn.

P—, Santa, 46 years old, from N. P.

The weight of the daily ration was 1172 grams; it is insufficient in respect to the various chemical component parts.

In this case, as can be seen in Table III, the balance is deficient and the losses are enormous. Only for potash there is a gain by 18.33%. All the other elements suffer a loss, 0.86% for nitrogen; the losses of the mineral elements are especially high. Indeed, we find a loss of 28.14% for salt, 68.01% for phosphoric acid, 202.55% for magnesia, 207.56% for lime, 55.86% for soda, and 36.13% for chlorine.

TABLE III.

Chemical Analysis of Foods Ingested.

	Weight, Gms.	Nitrogen, Gms.	Fats, Gms.	Carbohydrates, Gms.	Salts, Gms.	Phos. Acid, P^2O^5, Gms.	Magnesium, Mg O, Gms.	Calcium Ca O, Gms.	Potassium K^2O, Gms.	Sodium Na^2O, Gms.	Chlorine Cl, Gms.
Polenta	175	1.104	0.861	52.850	2.140	0.437	0.117	0.094	0.320	0.238	0.271
Bread	250	2.700	2.520	145.175	3.937	0.502	0.122	0.207	0.277	1.367	1.565
Milk	500	2.230	20.000	27.900	3.600	1.000	0.076	0.690	1.090	0.335	0.384
Rice	33	0,311	0.168	25.905	0.195	0.082	0.018	0.015	0.034	0.048	0.054
Macaroni ...	33	0.455	0 416	23.611	0.235	0.078	0.019	0.034	0.048	0.028	0.032
Beans	33	1.082	0.551	15.299	1.185	0.287	0.089	0.058	0.580	0.039	0.044
Sausage	30	0.840	19.893	.....	2.268	0.132	0.005	0.025	0.102	0.894	1.024
Salad	100	0.588	0.680	4.030	2.850	0.193	0.101	0.255	0.592	0.780	0.089
Olive Oil....	10	.....	9 995	.....	N. book	.....	.....	.....	.....	.....	.....
Salt	8	.....	.....	.....	8.000	.....	.....	.....	.....	3.145	4.854
Totals ..	1172	9.310	55.084	294.770	24.410	2.711	0.547	1.378	3 043	6.172	8.317

Comparison Between Ingestion and Elimination During a Period of 24 Hours.

	Ingested, Gms.	Eliminated. Urine, Gms.	Eliminated. Feces, Gms.	Total Eliminated, Gms.	Balance. Gain, Gms.	Balance. Loss, Gms.	Bal. Per Cent. of Materials Ingested. Gain, Gms.	Bal. Per Cent. of Materials Ingested. Loss, Gms.
Nitrogen	9.310	7.120	2.270	9.390	.....	**0.080**	.....	**0.86**
Fats	55.084	.....	11.305	11.305	**44.779**	.....	**81.28**	.....
Carbohydrates	294.770	.....	14.487	14.487	**208.283**	.....	**95.18**	.....
Salts	24.410	17.500	13.781	31.281	.....	**6.781**	.....	**28.14**
Phosph. Acid (P^2O^5)....	2.711	1.250	3.305	4.555	.....	**1.844**	.....	**68.01**
Magnesium (Mg O).....	0.547	0.140	1.515	1.655	.....	**1.108**	.....	**202.55**
Calcium (Ca O).....	1.378	0.087	3.600	3.687	.....	**2.309**	.....	**267.56**
Potassium (K^2O).....	3.043	1.350	1.135	2.487	**0.558**	.....	**18.33**	.....
Sodium (Na^2O).....	6.172	8.010	1.610	9.620	.....	**3.448**	.....	**35.86**
Chlorine (Cl)	8.317	9.439	1.823	11.322	.....	**3.005**	.....	**36.13**

INDIVIDUALS WITH ACTIVE PELLAGRA (TABLE IV).

Nourishment principally from corn.

P—, Anna, 50 years old, born T. As in the preceding case (Table III), the daily ration of 1230 grams is insufficient with respect to its chemical component parts.

The balance shows in this case still greater losses than in the case of Table III. Indeed, there is here an enormous deficit for

all the elements. The losses are 54.28% for nitrogen, 29.78% for salt, 96.77% for phosphoric acid, 171.25% for magnesia, 431.14% for lime, 14.15% for potash, 55.47% for soda, 31.60% for chlorine.

TABLE IV.

Chemical Analysis of Foods Ingested.

	Weight, Gms.	Nitrogen, Gms.	Fats, Gms.	Carbohydrates, Gms.	Salts, Gms.	Phos. Acid, P^2O^5, Gms.	Magnesium, Mg O, Gms.	Calcium Ca O, Gms.	Potassium K^2O, Gms.	Sodium Na^2O, Gms.	Chlorine Cl, Gms.
Polenta	800	5.048	3.963	241.600	10.099	2.000	0.536	0.432	1.464	1.403	1.500
Milk	200	0.892	8.000	11.160	1.440	0.400	0.030	0.267	0.436	0.134	0.153
Rice	50	0.471	0.255	39.250	0.343	0.125	0.028	0.023	0.051	0.073	0.083
Beans	50	1.640	0.835	23.180	1.795	0.435	0.136	0.088	0.879	0.060	0.068
Sausage	25	0.700	16.377	.....	1.890	0.110	0.004	0.020	0.085	0.745	0.850
Salad	45	0 265	0.306	1.813	1.282	0.087	0.045	0.114	0.266	0.035	0.040
Cheese	40	1.588	11.040	0.640	2.080	0.472	0.027	0.459	0.055	0.614	0.700
Olive Oil.....	10	.....	9.995	N. book	.....	.....	.....	.....	.....	.....	.....
Salt	10	.....	.....	.....	10.000	.....	.....	.....	.....	3.932	6.068
Totals ...	1230	10.604	50.944	317.643	28.929	3.629	0.806	1.412	3.236	6.996	9.462

Comparison Between Ingestion and Elimination During a Period of 24 Hours.

	Ingested, Gms.	Eliminated.		Total Eliminated, Gms.	Balance.		Bal. Per Cent. of Materials Ingested.	
		Urine, Gms.	Feces, Gms.		Gain, Gms.	Loss, Gms.	Gain, Gms.	Loss, Gms.
Nitrogen	10.604	10.820	5.540	16.360	.....	**5.756**	.....	**54.28**
Fats	50.944	.....	13.200	13.200	**37.744**	.....	**74.09**	.....
Carbohydrates	317.643	.....	19.140	19.140	**298.503**	.....	**93.97**	.....
Salts	28.929	20.450	21.125	37.544	.....	**8.615**	.....	**29.78**
Phosph. Acid (P^2O^5)..	3.629	0.720	6.421	7.141	.....	**3.512**	.....	**96.77**
Magnesium (Mg O)...	0.806	0.163	2.026	2.189	.....	**1.382**	.....	**171.25**
Calcium (Ca O).....	1.412	0.100	7.385	7.485	.....	**6.072**	.....	**431,14**
Potassium (K^2O).....	3.236	1.577	2.118	3.695	.....	**0.458**	.....	**14.15**
Sodium (Na^2O).....	6.996	9.630	1.247	10.877	.....	**3.881**	.....	**55,47**
Chlorine (Cl)	9.462	11.030	1.422	12.452	.....	**2.990**	.....	**31.60**

If Tables III and IV representing active pellagra, are compared, with Table I, representing the normal individual, and Table II, representing one formerly pellagrous, we find that there is an enormous difference between the balance of persons with active pellagra and

the other two. Indeed, we find in pellagrins great losses of nitrogen, and particularly of the salts, phosphoric acid, magnesia and lime. The conclusion, then, could be drawn that, in case of pellagrins, there is a marked loss of nitrogen and of the mineral elements.

A comparison of these tables allows us to fix the value of the results from Tables V and VI.

NONPELLAGROUS INDIVIDUALS (TABLE V).

Mixed diet.

(Denutrition of advanced type with enormous losses of mineral substances.)

This table and the following (VI) cover the cases of two patients suffering from general weakness, gastro-enteric and nervous disorders and advanced denutrition. These patients, belonging to the rich class, have always had varied diet, which included meat, broth, milk, legumes, pastry, greens, fruit, bread, wine, sweets, cocoa, cheese, butter, coffee, tea.

Let us examine the case of Table V.

M—, Th., 48 years old. Advanced denutrition with great losses of the mineral elements.

The weight of the daily ration was 1440.95 grams. As in all the cases under our observation, this ration was given for three days.

The alimentary balance, in this case, shows marked losses of nitrogen, salts, phosphoric acid, lime and potash. Only three represent gain: magnesia, with 13.47%; soda, with 2.52%, and chlorine, with 1.34%.

The very great losses are: 23.11% for nitrogen, 20.41% for salt, 44.52% for phosphoric acid, 28.19% for lime, and 5.07% for potash

TABLE V.

Comparison Between Ingestion and Elimination During a Period of 24 Hours.

	Ingested, Gms.	Eliminated.		Total Eliminated, Gms.	Balance.		Bal. Per Cent. of Materials Ingested.	
		Urine, Gms.	Feces, Gms.		Gain, Gms.	Loss, Gms.	Gain, Gms.	Loss, Gms.
Nitrogen	8.790	10.160	0.662	10.822	.....	2.032	.....	23.11
Fats	70.800	.....	1.720	1.720	69.080	.....	97.57	.....
Carbohydrates	147.820	.....	3.280	3.280	144.540	.....	97.78	.....
Salts	14.440	15.750	1,630	17.389	.....	2.949	.....	20.41
Phosph. Acid (P^2O^5)	1.572	1.620	0.651	2.271	.....	0.699	.....	44.52
Magnesium (Mg O)	0.291	0.098	0.153	0.251	0.040	.....	13.47	.....
Calcium (Ca O)	0.383	0.208	0.283	0.491	.....	0.108	.....	28.19
Potassium (K^2O)	2.166	1.934	0.342	2.276	.....	0.110	.....	5.07
Sodium (Na^2O)	5.257	4 919	0.205	5.124	0.133	.....	2.52	.....
Chlorine (Cl)	5.969	5.712	0.327	6.039	0.070	.....	1.34	.....

NONPELLAGROUS INDIVIDUALS (TABLE VI).

Mixed nourishment.

(Advanced denutrition with enormous losses of mineral substances.)

Madame B—, 42 years of age.

The weight of the daily ration was 1593 grams.

In this case, with the exception of a gain of 10.98% for magnesia ingested, the losses of all the (other) elements are greater than in the preceding table (V). Indeed, we find a loss of 53.59% of nitrogen, 29.61% of salt, 27.05% of phosphoric acid, 6.71% of lime, 40.14% of potash, 120.86% of soda, and 128.18% of chlorine.

TABLE VI.

Comparison Between Ingestion and Elimination During a Period of 24 Hours.

	Ingested, Gms.	Eliminated.		Total Eliminated, Gms.	Balance.		Bal. Per Cent. of Materials Ingested.	
		Urine, Gms.	Feces, Gms.		Gain, Gms.	Loss, Gms.	Gain, Gms.	Loss, Gms.
Nitrogen	7.390	10.410	0.930	11.340	.....	**3.950**	.....	**53.59**
Fats	29.780	.....	3.350	3.350	**26.430**	.....	**88.75**	.....
Carbohdyrates	203.420	.....	3.250	3.250	**202.170**	.....	**99.38**	.....
Salts	19.210	22.520	2.380	24.900	.....	**5.690**	.....	**29.61**
Phosph. Acid (P^2O^5)	1.848	1.740	0.607	2.347	.....	**0.499**	.....	**27.05**
Magnesium (Mg O)	0.446	0.167	0.230	0.397	**0.049**	.....	**10.98**	.....
Calcium (Ca O)	0.700	0.352	0.395	0.747	.....	**0.047**	.....	**6.71**
Potassium (K^2O)	2.628	3.245	0.438	3.683	.....	**1.055**	.....	**40.14**
Sodium (Na^2O)	3.600	7.716	0.235	7.951	.....	**4.351**	.....	**120.86**
Chlorine (Cl)	3.974	8.805	0.263	9.068	.....	**5.094**	.....	**128.18**

If we compare the two tables, V and VI, of the two patients that are nonpellagrous, with those of the pellagrins, we find that, in the cases of the two nonpellagrins a marked loss of nitrogen and of the mineral elements is found.

Has the demineralization of pellagrins a special character? If not, in order to examine the results of the elimination (urine and feces) in pellagrins and in nonpellagrous patients we should consider separately the elimination through urine and those through the feces in the two categories of patients, we arrive at the findings brought together in Table VII.

If we examine in this table separately the urinary and fecal elimination of the pellagrins and of the nonpellagrous demineralizations, we find enormous differences in the elimination in the two classes of patients. Indeed, in examining the elimination of nitrogen, of salts, of phosphoric acid, of magnesia, of lime, of potash, of soda and of chlorine, we see that in pellagrins the elimination through the urine is low in comparison with that which occurs through the urine in the two nonpellagrous demineralizations. In the latter the amount of urinary elimination is very large. On the contrary, through the fecal elimination we find in pellagrins enormous amounts in the columns of feces, in comparison with that of the fecal elimination of nonpellagrins. Then there are two classes of pellagrous and nonpellagrous patients; both are demineralized and

with great loss of the various elements. The minute examination of the elimination through the urine and feces permits us to differentiate these two classes of patients. The greatest part of the loss occurs *through the urine in case of nonpellagrins;* on the contrary, *in pellagrins* almost all the losses seem to be made through *the feces.* The absorption of the different elements is small, and this explains up to a certain point the marked diminution, in the urine of pellagrins, of nitrogen, the phosphates, magnesia, lime and potash.

TABLE VII.

Comparative Tables of Elimination Through Urine and Feces in Pellagrins and Nonpellagrins.

Pellagrins—Diet Largely of Maize—Percentage Elimination of Nitrogen and Mineral Substances Ingested.

	P. Santa (Table III.)		P. Anna (Table IV.)	
	Urine, Gms.	Feces, Gms.	Urine, Gms.	Feces, Gms.
Nitrogen	76.47	**24.38**	102.03	**52.24**
Salts	71.69	**56.45**	70.68	**73.03**
Phosphor. Acid ($P^2 O^5$)	46.10	**121.91**	19.84	**176.94**
Magnesium (Mg O)	25.59	**276.97**	20.19	**251.05**
Calcium (Ca O)	6.31	**261.25**	7.08	**525.01**
Potassium ($K^2 O$)	44.36	**37.30**	48.73	**65.39**
Sodium ($Na^2 O$)	128.16	**26.08**	137.65	**17.82**
Chlorine (Cl)	114.22	**21.91**	116.56	**15.02**

Nonpellagrins—Mixed Diet Without Maize.

(Cases with advanced denutrition and marked loss of mineral substances.) Percentage Elimination of Nitrogen and of Mineral Substances Ingested.

	Mr. Th. (Table V.)		Mrs. B. (Table VI.)	
	Urine, Gms.	Feces, Gms.	Urine, Gms.	Feces, Gms.
Nitrogen	115.58	**7.53**	140.86	**12.58**
Salts	109.07	**11.28**	117.23	**12.38**
Phosphor. Acid ($P^2 O^5$)	103.03	**41.41**	94.16	**32.84**
Magnesium (Mg O)	33.67	**52.57**	37.44	**51.57**
Calcium (Ca O)	54.30	**73.88**	50.28	**56.42**
Potassium ($K^2 O$)	89.28	**15.74**	123.46	**16.66**
Sodium ($Na^2 O$)	93.57	**3.88**	214.33	**6.52**
Chlorine (Cl)	95.69	**5.47**	221.56	**6.39**

Let us make an examination to determine in this table (VIII) how the urinary and fecal elimination in the normal individual

operates, as well as in the nonpellagrin (case of M—, Pietro, Table I) and in the former pellagrin (case of P—, Giulia, Table II).

These two persons used principally of corn diet.

For the normal, nonpellagrous individual we have seen (Table I) that the alimentary balance shows marked gains of almost all the elements. But if we examine the urinary and fecal elimination in detail, we find that in the column of the feces the numbers are very high in comparison with those of the column of the urines.

Considered from the point of view of certain elements, especially of phosphoric acid, of magnesia and of lime, it appears clear that there is a marked loss of these elements through the feces.

In the second case of this table (case of P—, Giulia) a person formerly pellagrous, we find likewise that the numbers of the column of the feces are very much higher than those of the column of the urines.

The fact, therefore, of high rates of fecal eliminations is observed not only in actual pellagra, in which the numbers are enormous, as we have seen, but likewise in *former pellagrins* (case of P—, Giulia) and also *in normal, nonpellagrous persons* (case of M—, Pietro). Let it be well understood that in these two classes of persons the elimination through the feces is not so high, but the fact found in the case of these persons, pellagrins and nonpellagrins, all being subjected to the same course of diet, appears thus the more evident.

TABLE VIII.

Comparative Table of Elimination by Urine and Feces in a Person Not Pellagrous and Normal and a Person Formerly Pellagrous.

Diet Largely of Maize—Percentage Elimination of Nitrogen and of Mineral Substances Ingested.

	Not Pellagrous. M. Pietro (Table I.) (Normal person.)		Formerly Pellagrous. P. Giulia (Table II.)	
	Urine, Gms.	Feces, Gms.	Urine, Gms.	Feces, Gms.
Nitrogen	66.38	**13.42**	75.28	**19.42**
Salts	42.01	**29.24**	84.94	**33.07**
Phosphor. Acid ($P^2 O^5$)	22.62	**67.26**	21.85	**85.62**
Magnesium (Mg O)	10.09	**115.51**	88.23	**123.76**
Calcium (Ca O)	3.23	**113.67**	3.71	**190.39**
Potassium (K^2 O)	24.01	**16.82**	47.52	**50.96**
Sodium (Na^2 O)	76.07	**4.52**	198.86	**4.29**
Chlorine (Cl)	75.39	**6.99**	164.78	**4.24**

As we declared at the beginning of this study, we do not desire, at present, to draw any conclusion. We intend to pursue this matter further and to extend our investigations over the largest possible number of cases. The work is long and tedious and not any too easy, because it exacts the greatest precautions in order that the results may be correct. It is in this spirit that we have labored, Grillo and I; the work and the time which these first researches have cost us suffice to excuse the small number of our observations.

Our later researches may enable us to modify the findings of our first observation; but for the present we are content to report, without any comment, the material facts which we have found and which we think may be fairly represented in the following résumé:

In order to determine the alimentary balance in pellagrins and nonpellagrins, we have administered the same nourishment for three days to the patients. This diet was, for all the cases, principally of corn. The daily ration, carefully weighed and analyzed, has shown all the chemical elements ingested. Again, we have collected the urine and feces for a period of three days, of 24 hours each, and have subjected them to a minute analysis. Then we established, for each person, the balance of each one of the elements ingested.

1. The alimentary balance of *the normal, nonpellagrous person* shows a gain with respect to all the elements ingested (with the exception of magnesia and lime, which show a slight loss).

2. The alimentary balance *of a former pellagrin* has shown slight losses for salts, phosphoric acid, magnesia, lime, soda, chlorine, and a gain for nitrogen and potash.

3. The alimentary balance for an *individual with active pellagra* shows enormous losses of all the elements. These losses were, in one case, 54.28% of nitrogen, 96.77% for phosphoric acid, 171.25% for magnesia, 431.14% for lime.

4. Similar losses show themselves in other pathologic states. In two cases with advanced denutrition, in nonpellagrous individuals, always on an abundant mixed diet, we found very high losses of nitrogen and the mineral elements.

In these individuals the greater part of the losses occurred *through the urine;* in case of pellagrins, on the other hand, with the exception of soda and chlorine, the proportion of the elements *eliminated through the feces* is enormous, in comparison with that eliminated through the urine.

5. We have likewise found very high figures for eliminations through the feces in case of *those formerly pellagrous* and in *normal, nonpellagrous individuals.*

High losses *through the feces* are observed, therefore, not only in active pellagra, *but also in normal, nonpellagrous persons.*

From the above exposition we may suspect the preparatory action of improper diet in the development of the existing disturbances of metabolism which we found, but later observations will permit us to formulate, we hope, more precise conclusions.

ANAPHYLACTIC REACTION IN PELLAGRINS AFTER INOCULATION WITH AQUEOUS EXTRACT OF SPOILED CORN.*

A report based upon researches by Dr. Guido Volpino, Professor of Bacteriology, with the Collaboration of Drs. A. Mariani, E. F. Bordoni, and L. Alpago-Novello, of the Institute of Hygiene (Pro fessor L. Pachiana, Director), University of Turin, Italy.

[*Editorial Note.*—This brief but important paper, submitted by Professor Volpino and his associates, represents the general conclusions of experimental work of which reports have already been published in very recent numbers of the *Revista di Igiene e di Sanita Publica.* If their conclusions can be confirmed by other workers in this field, it would lead us to hope that decided progress has been made in the study of pellagra. Work of this character must make a strong appeal to American students of the disease. For full details the reader is referred to the original articles.]

1. Persons suffering from pellagra, when inoculated under the skin or into the muscles, with a certain quantity of aqueous extract of damaged corn, insufficient to produce appreciable phenomena in the majority of non-pellagrins, present, with rare exception after a few hours, a reaction of hypersensibility, which in some cases is very marked. Such a reaction manifests itself either by stupor. somnolence or semi-comatose states, or by striking psychical and nervous excitability. In both cases these phenomena are accompanied by a remarkable increase of the pulse rate, dyspnea, rise of temperature, even to 40 degrees centigrade; often also by vomiting and increased peristaltic action, with bloody diarrhœa, and sometimes by intensification of pre-existing erythemas.

2. The difference in the reaction to such inoculations in pellagrins and non-pellagrins is very marked. The latter do not appreciably present any reaction in a large majority of cases, even when treated with doses eight or ten times greater than the minimum dose necessary to produce evident reaction in pellagrins.

*This article also appears in the Transactions of the Fifteenth International Congress on Hygiene and Demography, Washington, 1913, p. 344.

3. The hypersensibility demonstrated in pellagrins by inoculation with this aqueous extract of spoiled corn has specific characteristics which cannot be obtained by injecting extracts of good corn.

4. The active substance which causes the reaction to aqueous extracts of spoiled corn is obtained by adding one volume of the well-ground grain to three or four volumes of normal salt solution. Keeping this mixture at 55 degrees centigrade for six hours in a water bath, then filtering and adding to the filtrate 20 times its volume of absolute alcohol. There results a white precipitate of the active substances.

5. The active substance, thus obtained, to which we have given the name of "pellagrogenina," is soluble in water but not in alcohol. It does not lose its activity after exposure to a temperature of 110-115 degrees centigrade; has only a slight degree of toxicity either for experimental animals, or, in a general way, for healthy human beings, while it is, on the contrary, positively toxic for pellagrins.

6. The characteristic reaction which appears in pellagrins after the injection of aqueous extract of spoiled corn, also appears after the injection of "pellagrogenina" in appropriate dosage and is even more marked and more specific after injecting "pellagrogenina" in proper aqueous solutions. This substance when injected in a pure state in non-pellagrins has never given appreciable reaction.

7. The results obtained from 84 experiments performed with this substance, lead us not only to conclude that there is some specific etiological relation between spoiled corn and pellagra, but also induce us to suggest the use of this reaction as a practical procedure in the diagnosis of pellagra itself. (Included in the 84 tests are the 71 published in the *Revista d'Igiene* and 13 experiments not yet published but which will appear in a short time.)

To obtain a safe and appreciable specific reaction in persons suspected of having pellagra, it is sufficient to make one injection of 1 to 2 c. c. of a 10 per cent. aqueous solution of pellagrogenina sterilized at 110 degrees centigrade for ten minutes.

8. Having established a specific reaction in pellagrins to pellagrogenina, suggests attempting a prophylactic treatment of pellagra by immunization with successive injections of this substance in gradually increasing doses.

III. Local History and Diagnosis of Pellagra

PELLAGRA IN RHODE ISLAND.

By ARTHUR H. HARRINGTON, M. D., Superintendent State Hospital for the Insane, Howard, R. I.

The scope of this paper is purely historical and attempts to state, as far as the writer has been able to determine from the data available, the extent of the prevalence of pellagra in Rhode Island.

The subject will first be considered under the head of Pellagra in Relation to the State Hospital for the Insane.

The hospital is situated upon rising ground at a height of about 75 feet above sea level. It is at the lower end of the Pawtuxet Valley, about one mile distant from the Pawtuxet River, a rather sluggish stream which flows through this valley. Upon the borders of this stream for several miles are mills and mill villages. This river furnishes the water supply for the hospital and is, as well, a source of the water supply of the city of Providence. The public waterworks have a filtering plant which pumps this water. The water furnished to the hospital is from these same waterworks.

The hospital is located about seven miles from the heart of the city of Providence, in a sparsely settled open country. Adjoining the hospital premises are the grounds upon which are located other institutions of the State, viz.: the State Almshouse, the State Workhouse and House of Correction, and the State Prison.

The State Hospital for the Insane has over 1,400 inmates and employees. The other institutions named have about 1,000 inmates and employees. These institutions are all located within a stone's throw of each other and have a total population of about 2,400 persons.

Upon the farms belonging to these institutions are raised large quantities of succulent vegetables—tubers, roots and leguminous products which are consumed by the inmates and employees.

One product of the farms is rye, the grain of which is threshed out, roasted and furnishes, in place of coffee, a drink for the inmates.

In respect to the use of this rye, as a substitute for coffee, we are probably an exception to the majority of institutions.

The rye when harvested is stored in our lofts and threshed as needed throughout the year. Rye has been raised and used for making a beverage for the inmates for years at Howard.

All other foods with the exception of some pork, which we raise, are bought in the market.

In the summer of 1910 a case of pellagra occurred among the patients of the State Hospital for the Insane. This was the first case which any of the medical staff connected with the hospital had ever seen and recognized at the same time. Following this more cases developed among our patients during the summer of 1910. We asked Dr. Gardner T. Swarts, Secretary of the State Board of Health, to see these first cases and he confirmed our diagnosis.

Between the summer of 1910 and the month of August, 1911, the symptoms of pellagra, gastro-intestinal and neurological, together with the well marked skin lesions, appeared in 21 patients. Ten of these have died from the disease. These twenty-one cases have been made the subject of study by two of the hospital staff, viz.: Dr. E. H. Cohoon and Dr. Frederick J. Farnell. The full report of these cases, with that of the clinco-pathological work done by Dr. Farnell upon them, will probably appear soon in an issue of the *Boston Medical and Surgical Journal.*

Subsequently to these 21 cases there appeared between August, 1911, and October 1st of the year 1912 eleven additional cases, with two deaths.

Thus we have had at the State Hospital for the Insane since the summer of 1910 thirty-two recognized cases of pellagra with 12 deaths, or a mortality of 37%.

Of these 32 cases, 27 were women and 5 were men, all white. In none of the cases were skin lesions observed at the time of admission. Consequently the diagnoses were all made subsequently to admission. Four of the cases were admitted since January 1, 1912; four in 1911; two in 1910; two in 1909, and the remaining twenty cases have been in the hospital for periods varying from four years to over twenty-five years. The longest residence in the hospital of any one of the cases, a case in which the disease appeared during the past summer, was twenty-nine years.

In preparing this account of pellagra in Rhode Island, an inquiry was started in order to ascertain if any evidence was obtainable as to whether any cases, unrecognized at the time, had ever existed in the State Hospital for the Insane previous to the appearance of our cases in 1910.

Upon this point the following information has been gained: Dr. George E. Simpson, who has been connected with this hospital since 1905, states that a female patient in his service, who had been a resident of the hospital for five years, in the summer of 1908 developed skin lesions upon the hands. She passed rapidly into a cachectic state with diarrhœa and died in a short time. Dr. Simpson now states that in the light of present information gained in observing our recent cases of pellagra, he has no hesitation in expressing his belief that this case was one of pellagra. He further states that he has a distinct recollection of seeing here a few other cases in the years between 1905 and 1910, probably as many as six at least, who presented the same picture as our recent cases now recognized as pellagrins, and that the skin lesions at the time caused considerable discussion among the members of the medical staff. While the lesions were looked upon as sun burns, yet even then that explanation did not seem satisfying. As pellagra was not known to have existed in Rhode Island that disease was not thought of.

Dr. Harry W. Kimball, of Providence, Rhode Island, Surgeon to the Department of the Skin at the Rhode Island Hospital (general hospital), who was an interne at the State Hospital for the Insane in 1891, has permitted me to state that during his service at the latter institution he recalls distinctly observing a few inmates who exhibited skin lesions, which, in the light of his present information concerning pellagra, he has no hesitancy now in declaring to have been cases of pellagra.

From these data we have, I believe, unquestionable evidence that pellagra has existed among the patients at the State Hospital for the Insane as far back at least as 1891. The evidence seems to lead to the conclusion that for the years from 1891 to 1910 there were occasional cases of the disease, while from 1910 to the present date we have had an approach, at least, to an epidemic of pellagra.

I will next consider pellagra in relation to other State institutions at Howard.

Dr. Henry A. Jones, the resident physician of the State Almshouse, State Workhouse and House of Correction, has observed five cases of pellagra in inmates of these institutions, four being males and one a female.

I am indebted to Dr. Jones for the privilege of studying the records of his cases and also for the opportunity of seeing some of them with him.

In the summer of 1910 Dr. Jones believed that he had a case of pellagra under his care. His diagnosis was confirmed by Dr. Gardner T. Swarts. This patient died of the disease July 11, 1910. This is the first case of which we have any record in Rhode Island, in which the disease pellagra was recognized as such, at the time, and it is the first instance in our State in which pellagra was entered as the cause of death.

Of the remaining four cases who came under the care of Dr. Jones three have subsequently died. Dr. Jones, therefore, up to the present date, October 1, 1912, records five cases with four deaths.

Finally: I will consider pellagra in Rhode Island in Relation to the Community at Large.

The first consideration under this inquiry was as to whether any of the cases of pellagra seen at the State institutions named above appeared to have the disease when admitted.

Of the 32 cases seen at the State Hospital for the Insane since the year 1910, there was not a single case in which the skin lesions were present when the patient was admitted and no evidence could be gathered to indicate that any one of these cases had at any previous time exhibited the skin lesions. Twenty-nine of these cases had been in the hospital for periods varying from five months to over twenty-five years, before the symptoms of pellagra were observed in them.

As a matter of record I will cite certain facts in relation to the remaining three of our thirty-two cases.

C. B., admitted May 10, 1912, showed the skin lesions on July 12th following. Mental symptoms were said to have appeared one week before admission. This patient has become demented quite rapidly and has also developed well marked neurological symptoms.

L. B., admitted March 18, 1911. Mental symptoms preceded admission by one month. On admission patient exhibited depres-

sion, restlessness and confusion. Diarrhœa followed two weeks after admission. Skin lesions appeared six weeks after admission. A second appearance of skin lesions appeared eight months after admission. The skin lesions this time were bullous and dark brownish-red. She then had convulsions, choreiform movements and died, death occurring nine months after admission and ten months after the beginning of mental symptoms.

C. M., admitted July 20, 1912, showed typical lesions eleven days later.

We shall never know the incubation period of pellagra until we have ascertained the cause. The cases are not frankly pellagra, I understand, until the appearance of the skin lesions, but looking back over the course of at least two of these cases, the mental symptoms, manifested previous to admission, were, not unlikely, the onset of the disease. If so, they came from the community bearing the disease when admitted to this hospital. I do not make this as an assertion—it is simply surmise.

Two of Dr. Jones' cases, however, afford positive evidence that they were the victims of the disease before their admission to the State almshouse. Both were residents of Rhode Island and had not previously been at any time at any one of the State institutions. One of the cases gave a clear history of the onset of the disease with skin lesions and other concomitants of the affection, for a period of five months previous to admission. This case terminated fatally. The second of these two cases entered the State almshouse, coming directly from the Rhode Island Hospital, from the service of Dr. Gardner T. Swarts, where the diagnosis of pellagra had already been made. This case also terminated fatally.

I am also permitted to refer to another case, diagnosed as pellagra, who was admitted to the Rhode Island Hospital. M. B., a woman, age 55, a resident of Providence, also a patient in the service of Dr. Swarts. As far as my information goes these are the only two cases which have been admitted to the Rhode Island Hospital in which the diagnosis of pellagra has been made.

I was invited recently by Dr. Jones to see a young woman whom a physician had brought to him for consultation, being suspicious that she was a pellagrin. This patient was 25 years of age and had resided in the Pawtuxet Valley for six years, coming there from Canada. Skin lesions had first appeared two years ago and were

typical of the chronic branny variety. They were well marked on both hands and arms, extending to the elbows. Of late the general health was beginning to be markedly impaired and she was evidently suffering appreciably from the toxic effects of the disease. There was no evidence of tuberculosis.

From these four cases I feel that there is positive evidence that pellagra is existent in the community at large in the State of Rhode Island, to some extent at least.

I will summarize my conclusions as follows:

First. Pellagra has existed at the State Hospital for the Insane at Howard, R. I., at least since 1891.

Second. Taking all the cases of all the State institutions at Howard of which we have definite record, the total number is 37, with 16 deaths, or a mortality of 40.5%.

Third. Pellagra is not confined to the locality of the State institutions at Howard, but it also exists in the community.

THE HISTORY OF PELLAGRA IN THE STATE OF NEW YORK.

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This chapter in the history of pellagra is brief and soon told. There has been very little of the disease in the State of New York. It has an interest in that, while little known till just of late, certain cases have in recent time come to light of which not less than three have appeared to be of native origin.

Not that it has been utterly unknown in the past, but by importation. In 1882 Dr. Samuel Sherwell, of Brooklyn, recognized a case of pellagra in an Italian sailor who came into hospital; and again in 1902 another, likewise an Italian sailor; both of these he has contributed to medical literature. They were fatal cases. In 1864 Dr. John P. Gray, Medical Superintendent of the Utica State Hospital for the Insane, reported in the American Journal for Insanity a case of pellagra coming to that institution, likewise a foreigner and fatal.

Attention having been drawn to pellagra by its extensive appearance in Peoria, the Medical Officers of the State Hospitals for the Insane have been alert for its discovery. I have made inquiry of all of them and find that at but one of the thirteen institutions, which total a large body of inmates, about 32,000, has any case been yet discovered. In the Kings Park State Hospital, Flatbush, of which Dr. William Austin Macy is Medical Superintendent, two cases have occurred, both of them women in early middle age, of foreign birth but for years residents of this country, and both had marked psychoses; their diagnosis may be questioned for the essential history of diarrhœa was not notably present. They occurred in 1910 and 1911; both were fatal.

There have been a few rumored cases, suspected of being pellagra, which on closer investigation prove not to be pellagra. I have made inquiry in regard to such in the cities of Binghamton and Elmira, near the Pennsylvania line, and there is no reason to believe that in either there has been a case of this disease.

Dr. Howard Fox, of New York, reports a case of pellagra which he brought from Georgia for the purpose of demonstrating it before

the Academy of Medicine and to call the attention of the medical profession to the prevalence of the disease and its possible development over wider areas. In his report he makes reference to an undoubted case of pellagra seen by Dr. John A. Fordyce in the city hospital and to another seen at the Marine hospital by Dr. Claude Lavinder; these were casual cases from an outside source.

Dr. A. Caccini, of New York, makes a report in the Medical Record of March 11, 1911, of eight cases seen in dispensary and private practice within the last few years. These were all of foreign origin save one. This one was a native of New York and had always lived in the city; he had a history of pellagra of six years' duration, had not been corn fed, and came to the clinic for pulmonary tuberculosis. This is the first case of which I find record in which the subject was an American, a native resident of this State, and without history of a possible foreign origin.

A pellagrous subject, a Russian, seven years in this country, 35 years of age, died in Bellevue Hospital July 13, 1912, of pneumonia.

Dr. Grover Wende, of Buffalo, has reported recently a case of pellagra. The subject was a native of this country and had never been far from her home in Buffalo; she had always been well nourished and corn had not specially been an article of diet. Her ailment began in 1906 with psychic disturbance and diarrhœa and continued till the present time, with abatement in cold weather, digestive disturbances with enfeeblement and depression returning in the summer, and skin lesions in the last two summers. She had, in 1910, pronounced symptoms of pellagra affecting the alimentary tract, the cerebrospinal system and the skin in a classic way and she died the following autumn after an access of them. (Copy of Dr. Wende's report accompanies.)

I myself saw this year, and made report thereon to the State Department of Health, a case likewise indigenous to this State. It was one of very short duration, but with the leading characteristic symptoms.

The subject was an American woman, aged 43, of lowly pedigree and surroundings, illiterate and having had a life of poverty and deprivation accentuated during the last two or three years by reason of desertion by her husband and hard struggle for the maintenance of herself and small children. She had subsisted largely on corn meal of late, purchased from the ordinary market supply. She was

born in Hornell, a small city, and had probably never been beyond the limits of her native county.

I saw her in June last with her attending physician, Dr. F. C. Robbins, who has had a service as physician in a State Hospital for the Insane and was therefore the more ready to suspect pellagra. She was slight and emaciated, weighing less than 100 pounds; there was marked languor, apathy and dullness of mind, but she was intelligent when aroused; the knee reflexes were exaggerated; there was a staring look due to exophthalmos with thyroid enlargement; her blood pressure was 140, pulse 100, hemoglobin 60. The tongue was lightly coated, the edges red; gums not swollen; diarrhœa; abdomen flaccid and insensitive. The entire dorsum of the hands and fingers were dull red, as of mahogany stain with a bright red showing through, a peculiar type of redness which I have never seen in any ordinary dermatitis; the skin was thickened and edematous, in patches rough as from papillary engorgment; there were a few soft lactescent vesicles; there were no free areas and the lesion terminated abruptly at the palmar juncture; there was bracelet arrangement about the wrists of the same morphology but more active; the arms were not involved and there were no lesions on the arms nor elsewhere, none on the face or neck.

The history of the case was that during the past winter she had been subject to diarrhœa, digestive disturbance and inappetence, which became more pronounced in the spring; at which time she became depressed and mentally dull, and indisposed for effort and was enfeebled; at the same time the erythema appeared on the hands.

Later there was access of the diarrhœa and prostration and she died a few weeks after I saw her, the entire course of her disease coming within six months.

There is at present no known case of pellagra in the city nor in the State of New York.

It is improbable that any case will be overlooked if at all well marked by those who keep it in mind and are looking for it. To the mass of the medical profession of this State it is an unknown disease, and it is entirely possible that cases may occur or exist which have not been recognized.

Of the 16 cases to the present time of which I have obtained information, all have been in foreigners and of foreign origin save

three, namely: one of the cases reported by Dr. Caccini; the one reported by Dr. Grover Wende; and the one of which I have here made report. Health authorities will all be interested in whatever may be gained regarding pellagra, and surely aid in its investigation.

PELLAGRA IN OHIO.

By A. RAVOGLI, M. D., Professor of Dermatology, College of Medicine, University of Cincinnati.

It is with great satisfaction that I can state that pellagra in Ohio so far is exceedingly rare. For many years never has come under my observation a case of pellagra in my private practice, neither in the hospital service. It was only the summer of 1912 that through the kindness of Dr. H. Hoppe, neurologist in the city hospital, I had under my study the first case of pellagra, in its beginning. The man was in the neurological service for mental derangements. He showed a very marked erythema of the back of both hands extending to the lower third of the forearm with a sharp line of demarkation between the normal and the affected skin. A small patch of erythema on the nose, forehead, and neck. The man came from West Virginia, but for nearly four years had made Cincinnati his home. His occupation was tinner and used to repair tin roofs in the country. His illness begun four weeks before coming to the hospital, with general bad feeling, loss of appetite, pain in the stomach, occasional vomiting and obstinate diarrhœa. He became very nervous, and suffered with insomnia. His memory failed so much that he could not remember where he was. Just at that time the dorsal region of both hands from the second phalangeal joints to a little above the wrists became intensely red and slightly swollen. Later on the skin became dry, cracked and would peel off. He never complained of itching, although at times would complain of a burning sensation. He was questioned on his diet, especially on the use of cornmeal. He had eaten cornbread, but not as an exclusive staple food. The principal complaints were the diarrhœa and a sense of heavy feeling in the epigastric region.

His mental condition in the hospital improved, and he could answer questions freely, but was only somewhat confused and often mistook one day for another. The pupils were slightly irregular, and reacted sluggishly to the accommodation. A little tremor of the muscular system, and the least noise startled the patient considerably. Feces were examined without finding entamaba coli. Wessermann also was negative.

There was no doubt that it was an incipient case of pellagra, which so far is diagnosed only on its clinical symptoms. We have at present no positive sign, neither from the feces, nor from the blood to enable us to establish a positive diagnosis.

Another case of pellagra affecting rather severely the back of the hands and the forehead was seen by me through the courtesy of Dr. F. W. Langdon, consulting physician in the Cincinnati Sanitarium for mental diseases. It was in a lady in her fifties, who on account of her mental disorders had been placed in that institution. She belonged to a well-to-do family. Her home was in Kentucky, but she often resided with her daughter in Pittsburgh.

There has been referred to me the serious condition of the sister of an Ohio physician, who has been declared to have pellagra. She is married and has lived in West Virginia for many years.

Drs. Corlett and Schultz have reported a case of pellagra which occurred in a woman who died in Cleveland City Hospital. She had been admitted in the hospital twice before the diagnosis of pellagra was established, suffering with stomach trouble, vomiting and peculiar skin eruptions. The woman died and a post morten was allowed. The most important pathological changes were mostly of the nerve cells, and the nervous system which had been primarily attacked, giving a pathological group of symptoms revealed by mental impairment, gastro-intestinal involvement, and symmetrical skin lesions. It is possible that in Ohio may exist some other cases of unrecognized pellagra, but from the descriptions, and from the attention given to the skin eruptions any case would be found out in short time.

We can say, therefore, that with the exception of these few sporadic cases, the State of Ohio can be called immune from pellagra.

I find it yet difficult for me to change my opinion that fungi vegetating as saprophytes in the corn or probably in the grains may be responsible for this disease. It is possible that the inquinated (?) water containing fungi or palmallæ may be responsible for the production of this disease. But after the works of Volpino* on the anaphylactic reaction in pellagra patients by inoculation of watery extract of spoiled maize, we must recognize that the Italian observers

*Volpino Guido. Transactions of the Fifteenth International Congress on Hygiene and Demography. Vol. II, p. 344.

have not been on the wrong trail. In fact, Volpino has observed that pellagra patients when inoculated with a small quantity of watery extract of spoiled maize, either under the skin or deeply in the muscular masses, after a few hours show accentuated reaction of hypersensibility, in form of dullness, drowsiness and semicoma, or by strong nervous excitability. These phenomena are accompanied by a remarkable acceleration of the pulse, dyspnea, rise of the temperature, sometimes vomiting, tenesmus, accentuation of the preexisting cutaneous eruptions.

This reaction is not obtained in any one who is free from pellagra, even if the injection is given with much larger quantity of the watery extract of spoiled maize. The same patients have been injected with watery solution of sound maize, without showing any hypersensibility.

The deteriorated maize infected with that characteristic mould, was kept in a solution of chloride of sodium, in bagno marie, then treated with alcohol, giving a precipitation of white flakes. This is soluble in water, and not in alcohol, and was called by Volpino pellagrogenin. It has a slight degree of poisoning for animals and for the sound man, but is decidedly poisonous for pellagrins. This poisonous property is maintained even if the solution is exposed to the temperature of 110 to 115 degrees C.

The experiments have been repeated in nearly one hundred cases with constant results, and they consider it of great efficiency in the pathogenesis of pellagra, and have proposed it as an anaphylactic reaction for the diagnosis of pellagra.

If this method of diagnosis is confirmed, the etiology of pellagra from spoiled maize is an assured fact and its prevention will be easily applied.

That some varieties of flies are the cause of a great many diseases there is no reason to doubt. The arguments brought by Manson and Sambon, that the simulium reptans is the carrier of pellagra finds still a place in the etiological possibilities. Yet when we consider the early symptoms of pellagra, we find that they are mostly on the part of the digestive tract, and therefore it seems more plausible that the disease is carried by ingested food. Indeed the patients complain at first of a sour sensation in the throat and burning of the stomach, and then it is followed by incessant diarrhœa. For this reason I have not yet changed my views on the etiology of pellagra,

that fungi, may be *sporisorium maides,* or *aspergillus fumigatus,* etc., vegetating as saprophytes in spoiled corn, or possibly in other grains, may be responsible for the production of this dreaded disease. In the same way it is also possible that polluted water containing algæ, or fungi, may become the cause of this disease.

The idea at first expressed by Lombroso, and then maintained by Ceni, Corlett, Marie, Lavinder, Babcock and many others, of the toxic infective nature of this disease is proved by the clinical observation. Yet that this is the result of spoiled corn, although coherent with the entity of the disease, yet there are some weak points, which are sill waiting for proofs. The results obtained in Italy with the war against pellagra are very encouraging. In 1881 the statistics of the kingdom gave 103,981 persons affected with pellagra, and in 1889, the number descended to 72,925, and at present the number of cases is 36,329 for the whole of Italy. The diminution of the disease goes hand in hand with the agricultural improvements, and with the improved economic and hygienic conditions of the agricultural classes, and with the better preservation of corn, and with its limitation in alimentary use.

A commission from the counties' administration made compulsory the report to the health department of every case, and samples of corn were taken from each crop and from the different localities, for chemical and bacteriological study. Public lectures were given on hygiene, on the methods of preserving food substances. Public kitchens were established to distribute food well prepared, at low prices. The water supply was also subject of study and it was improved when necessary. With these rules Italy has obtained splendid results.

I must repeat my first statement that pellagra in Ohio does not exist, the few cases reported were sporadic and from persons coming from other States. It is, however, necessary that the physicians know something about this disease, and if cases should be found, have them kept in institutions.

PELLAGRA IN WISCONSIN.

By O. H. FOERSTER, M. D., Milwaukee.

Pellagra as an epidemic disease is unknown in Wisconsin. With the exception of several imported cases, and one case apparently of local origin, there is no record of the disease in this State.

Mr. L. M. Hutchcroft, Statistician of the State Board of Health of Wisconsin, informs me under date of September 16, 1912, that "something like a year ago we endeavored to collect statistics on this disease for the entire State with especial reference to cases in the various institutions. The reports which we received from the various superintendents and health officers show that the disease is practically unknown in Wisconsin, with the exception of the imported cases. No cases were found in any of the institutions; neither had there been any history of the disease in any of the institutions."

In the fall of 1911, Dr. L. M. Warfield and the writer were given the privilege of examining the inmates of the Milwaukee County Hospital for the Insane with reference to pellagra, but no evidence of the past or present existence of the disease was discovered.

Newspaper reports of cases of pellagra in various parts of the State were declared unfounded by the local health officers, and it appears that the only recognized instances of the disease were four cases occurring in Milwaukee and reported by the writer in the Wisconsin Medical Journal, August, 1912.

The histories of these cases are as follows: One originated in Milwaukee, the other three were imported—one each from Arkansas, Indiana and Southern Europe, possibly Russia. Three proved fatal, and one has been lost sight of and had apparently recovered. All were typical cases, with cutaneous, gastro-intestinal, and nervous symptoms. One, a child of eight years, had eaten corn only in the form of corn flakes as a breakfast food, and had been away from the city only once, going then to Minneapolis. One was, according to his account, an escaped Russian political prisoner, who had lived for two years on a diet largely of corn. One was a farmer from southern Indiana, but his mental condition made an inquiry as to his previous history impossible. The fourth was a young man who undoubtedly acquired the disease in Hot Springs, Arkansas, and who had eaten corn at times.

Case 1. Girl, eight years of age; seen July 26, 1909, when she applied for admission to the Children's Free Hospital because of a persistent "sunburn" of eight weeks' duration. The sunburn had appeared during the first moderately warm days of 1909, as a rapidly spreading erythema located at first over the dorsum of the nose, then spreading to cheeks below eyes, and over dorsum of hands up to the knuckles, but not on the fingers. Within one week this erythema had spread over the entire face, except immediately surrounding the lips, and was marked on the left ear. On the dorsum of the arms and forearms an erythema with vesicle formation had appeared on July 18th and extended almost to the elbows. She was placed in the hospital.

Inquiry into the previous history showed that during July of 1907, the mother for the first time observed the presence of a very violent sunburn, limited to the face and hands, with slight vesicle formation, which disappeared within a few weeks. During the first warm days in 1908, after having been out of doors, the so-called sunburn reappeared in the same location, lasting about three weeks, with slight vesicle formation. During the remainder of the summer, the patient's skin remained without further inflammation, but showed some pigmentation. Until two years ago, with the exception of measles, during the winter of 1907-1908, the patient had always been well, but at this time began to be "pale and rundown" and showed definite mental depression. In the spring of 1909 patient had been sent home from school because she looked so poorly and has not been to school since. During the past month has had a constant diarrhœa, with pain at the umbilical region, and complains of pain and dryness of the throat. The child appears to be steadily growing weaker and never regains any strength. Frequently vomits without apparent cause and without relation to food.

During her stay in the hospital the dermatitis on face and hands subsided slightly, assumed a dark red color, exfoliated constantly for about six weeks, after which time the scaling continued only over the knuckles and dorsum of the hands, where the skin also was considerably thinned. While in the hospital in a screened bed, an erythema appeared in two dollar-sized patches symmetrically located on either side of the neck, in regions that had always been covered by her dress. Never showed an eruption on trunk or lower extremities. The general symptoms while in the hospital consisted of

a continuous diarrhœa, progressive loss of strength, anemia, increasing mental depression, occasional vomiting, and marked tremor of hands. The patient at times was up and about in the hospital, and, late in September, 1909, was discharged unimproved, except for the dermatitis, which had practically disappeared, leaving behind scaling pigmentation and atrophy of the skin on the dorsum of the hands. On the day of her discharge it was observed that after walking a short distance the body was inclined to the right side, with tenderness over the lumbar spine. Early in October, observed diplopia, which disappeared in three weeks. On standing there was a marked tremor of both legs. Four diarrhœic movements occurred daily and she became much emaciated. Hallucinations regarding persons were frequent, and the mental condition remained unimproved until death, on December 23, 1909.

Case 2. A Russian, male; about 35 years of age; seen at the Mt. Sinai Hospital by my associate, Dr. C. A. Baer, whose diagnosis I could confirm. When first examined by us (August, 1910) the patient was a typical example of fully developed pellagra; emaciated as the result of a long continued diarrhœa, semi-delirious, with a typical pellagrous eruption on hands, feet, neck, and face, the tongue superficially ulcerated and bleeding, and marked stomatitis. He shortly afterward unsuccessfully attempted to commit suicide by cutting his throat with a razor. After several months he apparently recovered, and according to last reports has remained well.

Case 3. A man, about 30 years of age; seen with Dr. L. M. Warfield at the Milwaukee County Hospital, during the summer of 1911. This patient had been an inmate of the institution during the winter of 1910-1911, and was affected with a generalized tuberculosis, especially involving the joints. Early in 1911 he went to Hot Springs, Arkansas, for three months, and shortly after his return, again entered the county hospital, where he developed the typical eruption of pellagra during July. Face, hands, wrists, elbows and feet were affected, his mentality was not clear, and he had a constant diarrhœa. It was not possible to determine with certainty if the bowel symptoms were due to pellagra or tuberculosis. This case ended fatally in October.

Case 4. A farmer, aged 73, from southern Indiana, seen with Dr. A. W. Akerly at the National Soldiers' Home. He had been an inmate for several months of an institution for the insane in

southern Illinois, and on arrival at the home had a marked diarrhœa, with abdominal pains, was much emaciated, semi-stuporous, and presented the characteristic eruption of pellagra on the hands, feet, wrists and neck. He died within a few days after admission. This case was of the chronic type, and had existed for five years.

It appears very improbable that Wisconsin will be numbered among the States in which pellagra can gain a foothold, but sporadic or imported cases, such as those cited, will doubtless be met with from time to time.

PELLAGRA IN MARYLAND.

By C. W. G. ROHRER, M. D., Maryland State Department of Health, Baltimore, Maryland.

INTRODUCTORY.

The preparation of this paper has been beset with difficulties, because pellagra is not a reportable disease in Maryland. But I have ever been wide awake to the occasion, realizing how important it is to note the appearance of pellagra in certain sections of our State. A fair proportion of the cases were reported voluntarily by physicians, while a careful watch has also been kept over the death records. Although these circumstances are not very favorable for completeness, I question very much if a single case of the disease has been omitted. I have not included the imported cases treated in our several hospitals, but have confined myself to cases of pellagra having their apparent origin within the confines of the State of Maryland.

While I do not wish to weary you with burdensome details, yet there are three Maryland conditions which I wish to discuss briefly before taking up the gist of my subject. These are:

a. The geographical features of Maryland.
b. Location and extent.
c. Climate and rainfall.

In order to draw conclusions from the Maryland cases of pellagra, a knowledge of the above topics is essential. I believe such information will help us toward a better understanding of the etiology of this disease.

GEOGRAPHICAL FEATURES.

Maryland, the "Old Line State," possesses an almost endless variety of geographical features. Its western part is traversed by the Alleghany and the Blue Ridge Mountains, important ranges of the great Appalachian chain whose lofty peaks tower high above the surrounding country. Slightly to the east and southeast of its center, the State is bisected by the Chesapeake Bay, an arm of the Atlantic Ocean famous for its oysters, its canvasback ducks, and other sea food and game. Its remote east forms part of the Mary-

land-Delaware Peninsula, reaching from Mason and Dixon's Line to the Atlantic Ocean.

Geographers usually divide Maryland into three regions, as follows:

1. The Coastal Plain;
2. The Piedmont Plateau; and
3. The Appalachian Region.

The Coastal Plain of Maryland forms the eastern part of the State, comprising the area between the Atlantic Ocean and a line passing from the northeastern corner through the city of Baltimore to the city of Washington, D. C. With the exception of the northwestern portion of Cecil county, the Coastal Plain includes all nine counties on the Eastern Shore of Maryland, namely: Cecil, Kent, Queen Anne, Caroline, Talbot, Dorchester, Somerset, Wicomico, and Worcester; and portions of Harford and Baltimore counties, practically all of Anne Arundel and Prince George's, and Charles, Calvert, and St. Mary's counties entire, of the Western Shore, the Chesapeake Bay dividing the State into shores.

The Piedmont Plateau of Maryland extends from the western limit of the Coastal Plain to the base of the Catoctin Mountains in Frederick county, comprising the greater part of Baltimore county, a narrow strip of land in the extreme north of Prince George's county, Carroll, Howard, and Montgomery counties in their entirety, and the eastern two-thirds of Frederick county.

The Appalachian Region forms the western part of Maryland, and comprises about one-fifth of the area of the State. The Appalachian Region includes all of Garrett, Alleghany, and Washington counties, and the western third of Frederick county.

LOCATION AND EXTENT.

The State of Maryland lies between 37 degrees 53 minutes and 39 degrees 44 minutes north latitude, and 75 degrees 4 minutes and 79 degrees 33 minutes west longitude. The total area of the State is 12,210 square miles, of which the land surface is 9,860 square miles. Its extreme length, east and west, is 240 miles and its breadth varies from less than three miles in Washington county, at the west, to about 125 miles near the meridian of 76 degrees.

The eastern section of the Coastal Plain, familiarly known as Eastern Maryland or the Eastern Shore, is in general less than

twenty-five feet above sea-level. In the Appalachian Region there are mountain peaks which rise to a height of 3,000 feet and more.

CLIMATE AND RAINFALL.

The climate of Maryland, as expressed by a local historian, is "temperate in summer and not violent in winter." This is true, in a general way. As the State is varied in its physical features, so it is correspondingly diverse in its temperature. In most places it is healthful; although the lowlands bordering the Chesapeake Bay and its estuaries were formerly malarious, on account of the mosquito-laden air of the marshes.

In the lower eastern and southern sections of the State the average temperature is 40 degrees in winter and 77 degrees in summer. In the higher lands to the west and north the average for winter is 27 degrees and for summer 70 degrees.

The annual rainfall varies from twenty-five to forty-eight inches, according to locality. Precipitation is heaviest on the eastern slope of the Catoctin Mountains, which range acts as a natural barrier to the moist easterly winds from the ocean, and on the shores of the Chesapeake Bay. In the more elevated regions to the westward of the State, the rainfall is less abundant. In general, the greatest precipitation occurs in the spring and the late summer.

NUMBER OF PELLAGRINS.

Down to the present writing (September 25, 1912) there have been 31 cases of pellagra accredited to the State of Maryland Nine of these individuals developed the disease in the city of Baltimore, while 22 were county cases. All have occurred in the Coastal Plain and in the Piedmont Plateau, where the rainfall is greatest and the soil composed of sands, clays, loams, and marls. Not a single instance of the disease has been found in the higher, drier, more elevated portion of the State known as the Appalachian Region.

HISTORICAL NOTE.

The first recognized case of pellagra in Maryland was seen by Dr. William S. Thayer, of the Johns Hopkins University, on the 18th of November, 1905. This patient presented a peculiar line of symptoms which were diagnosed pellagra by Dr. Thayer. The patient was a well-to-do white lady, aged 57 years, housewife by occupation, living about fifty miles from the city of Baltimore.

The second of the Maryland pellagra cases was also seen by Dr. Thayer, at the Johns Hopkins dispensary, May 14, 1909. A third case, a patient in the Mercy Hospital, Baltimore, admitted from Charles county, Maryland, was seen by the present writer on Saturday, August 7, 1909, and diagnosed pellagra.

CHRONOLOGY OF CASES.

The following concise summary of the 31 Maryland cases of pellagra might prove helpful and interesting. In addition to the date, I shall mention color, sex, and age.

Case 1. White female, aged 57 years. Improved, November 18, 1905.
Case 2. White male, aged 35 years. Improved, May 14, 1909.
Case 3. White female, aged 52 years. Died, August 20, 1909.
Case 4. White female, aged 55 years. Died, November 26, 1909.
Case 5. White female, aged 17 years. Died March 19, 1910.
Case 6. White female, aged 40 years. Died, April 12, 1910.
Case 7. White male, aged 61 years. Died, April 17, 1910.
Case 8. White male, aged 37 years. Died, April 28, 1910.
Case 9. White male, aged 54 years. Died, June 11, 1910.
Case 10. White male, aged 47 years. Died, July 19, 1910.
Case 11. White male, aged 77 years. Died, August 11, 1910.
Case 12. Colored female, aged 30 years. Died, September 6, 1910.
Case 13. White male, aged 10 years. Died, September 13, 1910.
Case 14. White female, aged 54 years. Died, February 9, 1911.
Case 15. White male, aged 64 years. Died, February 23, 1911.
Case 16. White female, aged 60 years. Died, March 23, 1911.
Case 17. White female, aged 64 years. Died, June 28, 1911.
Case 18. White female, aged 44 years. Died, July 5, 1911.
Case 19. Colored male, aged 65 years. Died, July 7, 1911.
Case 20. White female, aged 61 years. Died September 13, 1911.
Case 21. White female, aged 47 years. Died, September 26, 1911.
Case 22. Colored male, aged 11 years. Recovered, November 15, 1911.
Case 23. Colored male, aged 30 years. Died, November 17, 1911.
Case 24. Colored female, aged 6 years. Died, December 3, 1911.
Case 25. White male, aged 9 years. Died, December 27, 1911.
Case 26. White male, aged 35 years. Died, April 15, 1912.
Case 27. White male, aged 70 years. Died, May 10, 1912.

Case 28. Colored female, aged 42 years. Died, May 15, 1912.
Case 29. White male, aged 48 years. Died, June 14, 1912.
Case 30. White female, aged 29 years. Died, July 16, 1912.
Case 31. White female, aged 60 years. Died, August 24, 1912.

To summarize the Maryland cases of pellagra is interesting, to say the least. There have been a total of 31 cases, with the following results, arranged in three groups:

Group *a*. Terminated fatally, 28.

Group *b*. Improved, 2.

Group *c*. Cured, 1.

The one case under Group *c* was cured by the internal administration of urotropin.

Summed up by years, the following are the revised Maryland figures on pellagra:

1905.....1 case.
1906.....No case.
1907.....No case.
1908.....No case.
1909.....3 cases.
1910.....9 cases.
1911.....12 cases.
1912.....6 cases, down to date, making a total of 31 cases.

DISTRIBUTION AND LOCALITY.

In only one instance have two or more cases of pellagra occurred in one family in Maryland. It is that of Case 5 and Case 13, of the Maryland series of cases, in which a seventeen-year-old girl died in March and her ten-year-old brother in September.

As stated above, nine of the pellagra cases originated in the city of Baltimore and twenty-two in the smaller cities and towns and rural districts. The distribution of the twenty-two county cases is as follows:

Anne Arundel county..... 1 case.
Baltimore county ..... 6 cases.
Carroll county ..... 1 case.
Calvert county ..... 1 case.
Charles county ..... 2 cases.

Dorchester county	5 cases.
Queen Anne county	3 cases.
Somerset county	3 cases.

Other features concerning these cases will be set forth in a subsequent paper, entitled, "Clinical and Pathological Notes on Pellagra." Enough, however, has been said to convince the most skeptical that pellagra is more common in Maryland than is generally supposed.

CONCLUDING REMARKS.

While Maryland is fortunate enough not to possess a long series of pellagra cases, yet the fact that 31 cases of the disease have occurred within the limits of the State is sufficient grounds for a serious consideration of the malady by the State authorities. In view of the above conditions, the following conclusions may be formulated:

1. Pellagra should be made a reportable disease in Maryland. Its presence and almost uniform fatality make such a step highly advisable.

2. Pellagra prevails in Maryland where the greatest rainfall occurs and where the soil is composed of sand, clay, loam, and marl.

3. The geographical distribution of pellagra in Maryland is highly suggestive that warmth, moisture, and low altitude have an important bearing upon the etiology of the disease.

4. The telluric and climatic conditions of two of the three geographical divisions of the State of Maryland, namely, the Coastal Plain and the Piedmont Plateau, are favorable to the development of pellagra.

5. Nine of the thirty-one Maryland pellagrins developed the disease in the city of Baltimore; twenty-two developed the disease in the smaller cities and towns, in the suburbs of Baltimore, and in rural communities. In only a single instance has more than one case occurred in a family. The largest number of cases in any one community occurred in and near the city of Cambridge, Dorchester county.

6. While the pellagra problem is not alarming in Maryland, and I do not know of a single case of the disease at the present time, it certainly is deserving of unremitting attention.

7. Lastly, I believe a few sporadic cases of pellagra have existed in Maryland from the earliest times to the present. Formerly such cases were diagnosed eczema, sunburn, senile gangrene, arteriosclerosis, Raynaud's disease, leprosy, erysipelas, scurvy, purpura, etc. Today the pendulum has swung in the opposite direction, and cases of eczema, senile gangrene, symmetrical gangrene, leprosy, arteriosclerosis, Raynaud's disease, sunburn, erysipelas, and the like, are diagnosed pellagra.

NOTE.—I am indebted to Dr. James Bosley, Health Commissioner of the city of Baltimore, for much of the data concerning the city cases of pellagra.

PELLAGRA IN THE DISTRICT OF COLUMBIA.

By H. H. HAZEN, M. D., Washington, D. C., Clinical Professor of Dermatology, Howard University; Assistant in Dermatology, Johns Hopkins Medical School.

In October, 1911, Dr. S. R. Karpeles collected five cases of pellagra that had been treated in the District of Columbia in addition to reporting one of his own. Since that time five more cases have been under observation, only one of which, however, originated in the District. No fewer than six of these patients came from the neighboring counties of Virginia. So far three of these eleven patients have died, although I understand that the decease of another may be expected to occur at almost any time.

The one case that did originate in the District deserves study for several reasons, firstly, because no other case has originated here, and secondly, because of certain features associated with its origin.

On April 19, 1912, during my absence in Europe, a negro girl of seventeen was admitted to the service of Dr. E. H. Reede, at the Freedmen's Hospital, for supposed syphilis. Her history showed that since she was ten years of age she had not been out of the city for a single day until she was committed to the Girl's Reform School in October, 1911. She had lived between First and Second and E and F streets, N. W., in a squalid home, before admission. There was no history of any eruption, nor did the family, visitors, or neighbors appear to have thus suffered. She complained that at the school she was given no fresh meat, fowl, eggs, or fish; that in February, 1912, she had suffered from "rheumatism of the knees and bleeding of the gums," and that she had been hungry all of the time. About two weeks before admission, she began to feel bad, and had superficial inflammation around the vagina, as a result of which the school physician naturally diagnosed syphilis, a far from uncommon disease at the school.

A few days after her admission to the hospital, she showed a symmetrical erythematous eruption upon the hands, face, elbows, knees, and neck, and pellagra was at once suspected. When I returned home, May 5th, I confirmed this diagnosis. Because of her history of dietary insufficiencies, she was fed largely upon a

fresh protein diet, with, of course, the exclusion of corn. However, she grew progressively worse, and died May 19th.

None of our laboratory or clinical investigations, which we endeavored to make as thorough as possible, yielded any new information. Autopsy showed an active congestion of all organs, with a slight enlargement of the suprarenals, which, however, showed no microscopic change other than the congestion. We were unable to find the cell inclusions of Chalmers and Sambon in the brain tissue, although they were carefully searched for. It may be remarked that I was familiar with these inclusions, Dr. Sambon having kindly shown them to me at Rome, and that they certainly looked very like parasites.

The Girls' Reform School is situated in the extreme northwest corner of the District of Columbia, near the Potomac River and about three miles from Georgetown. It is well conducted and clean, uses city water, and is screened. Connected with it is a farm upon which fresh vegetables in abundance are raised. Inasmuch as most of the girls are committed for "crimes of passion," the board of trustees felt it wiser to give fresh meat but once a week, and then in the form of stews; meat gravy was frequently served upon the vegetables, however. Strange to say, no provision was made to serve fresh poultry, fish or eggs, some eggs, of course, being used in the cooking. While it is true that the inmates gained weight while at the institution, it is not surprising in view of the carbohydrate rich diet upon which they were fed. The vegetables were excellent, and the institution raised its own corn. It is gratifying that the president of the board had announced that the Marine Hospital Service would investigate conditions at the school.

This one case has brought up a number of very interesting questions. Firstly, did the disease originate at the school or at the home of the patient? In this section of the country pellagra is much more common in the rural districts, and so far as I can learn practically never occurs in those who have not been out of the city. More observations upon this point are desirable, for the question has never been seriously studied. Taken all in all the chances seem to me that the case originated in the school. Personally, it seems to me that the incubation period of pellagra is shorter than is usually believed, for I have seen children of two or three months with attacks in full bloom.

Secondly, when a disease occurs in an institution, what are the chances of more cases developing? Judging from the records of our insane asylums, almshouses and certain of the orphanages, as quoted by Dr. Rice, there is certainly far more than a mere chance of one case being the first and last.

Thirdly, was this the only case at the school? Two cases of skin lesions occurring at the same time were sent to another hospital where they were diagnosed syphilis, just as our case had been, and where they improved on anti-syphilitic treatment. In view of the general tendency to label all skin eruptions in the negro as syphilis, there remains the possibility that one at least of these two cases might have been pellagra. On the other hand, no new case of pellagra has originated in the institution.

Fourthly, what are the duties of the authorities in charge when pellagra is found to exist in an institution? It would seem to me that the food supply should be thoroughly overhauled in all respects; that the inmates should be inspected and watched, and that a careful search should be made for vermin. In the past we have found that our institutional diseases are usually spread by bad food or water, are due to animal parasites, or are transmitted by animal or insect carriers. In view of the fact that there is certain evidence to show that disease may be transmitted by one of the following parasites, the mosquito, the house fly, the stable fly—stomoxys calcitrans—the sand fly—simulium—or a tick of some kind, patients should certainly be isolated against insects of all kinds.

Fifthly, did a protein-poor diet in any way act as a predisposing influence favoring pellagra? It would seem that a diet insufficient in any substance might lower the resistance and make a more easy victim. In this regard, it is interesting to note that the Illinois Pellagra Commission states "Deficient animal proteid in the diet may constitute a predisposing factor in the contraction of the diesase."

Sixthly, is it wise to give growing young people a protein-poor diet on the supposition that it may increase the sexual appetite? There can be but one answer to this question, and that an emphatic No!

Seventhly, is pellagra on the increase around Washington? In view of the fact that all cases have been seen during the last two

years, although many well-trained men have been searching for several years longer, makes one feel that it is on the increase.

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THE GEOGRAPHICAL DISTRIBUTION OF PELLAGRA IN NORTH CAROLINA AND ITS SIGNIFICANCE.

By EDWARD J. WOOD, M. D., Wilmington, N. C.

Looking backward, it is readily appreciated just how important is the consideration of geographical distribution in the solution of problems of etiology of such diseases as malaria and trypanosomiasis. But in no disease have the boundaries of the endemic centres been so well defined as in pellagra in Italy. Since the earliest descriptions of this disease the areas of endemicity have remained unchanged. Until the published works of Sambon it had never occurred that there could be any geographical connection with the occurrence of the cases. Probably the first case of pellagra diagnosed in North Carolina was by J. B. Wright in the foothills of the Blue Ridge. The next recognition was by R. H. Bellamy on the very shore of the Atlantic Ocean. Bellamy's recognition, which was soon followed by the published report of Searcy in Alabama, cleared up for us many cases the diagnosis of which we had missed in the past. Some of our older colleagues recalled cases which they had seen many years before and had called by many different terms. After two years of observation Sambon's Progress Report appeared and I at once began a consideration of the large number of cases that had already come under my observation. It seemed a strong point against the theory of Sambon that pellagra should occur in Wilmington, which is less than eight miles from the ocean, and is also situated on the Cape Fear River, which is a tidal stream. On first thought it would seem that in the tidewater section there should be found no suitable breeding place for the fly in question because of the fact that rapidly flowing water is counted necessary for the aeration which is a requisite of the development of the eggs. On investigating these cases from the geographic standpoint it was evident that there were two classes of cases. The first and much larger was composed of country people who had recently moved into the city from the neighboring country districts. In many instances these people were found to be frequent visitors to their former neighborhoods. One of these families had four children under the care of R. H. Bellamy. All of these cases of pellagra developed

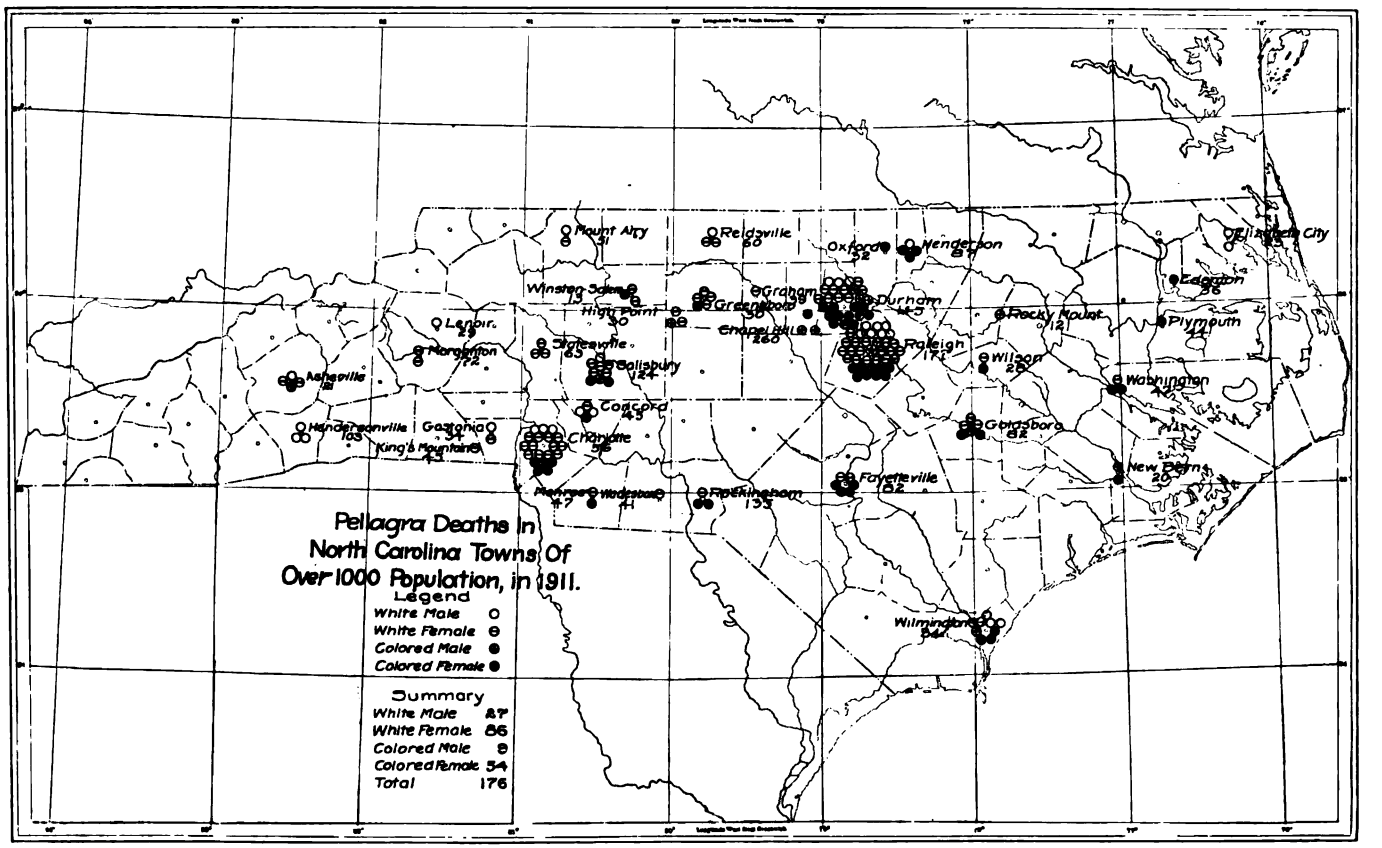
simultaneously. The parents were mulattoes of the better class and the children were well cared for. Another family of whites had six children simultaneously affected, and these, too, had within a few months come into the city from the country. Some of the patients who had always lived in the city gave histories of visits to the country. The second class of cases was composed of people who had lived in the city continuously without a visit to the country. There were some of these cases but the proportion was quite small. For some unexplained reason these victims were usually old, feeble people. It was found that city people were by no means immune from pellagra. This does not alter the fact, however, that the contention of Sambon is just as true here as in Europe, that pellagra is a disease of the rural population.

How to account for these cases occurring in the city in people who had not been in the country and who had never been away from home seems very difficult, and I am unable to find a reasonable explanation.

The accompanying map of North Carolina shows deaths from pellagra in towns of over 1,000 registration. It should be mentioned that this does not include deaths in the institutions of the State Hospital for the Insane. It is seen from this map that pellagra occurs only very infrequently in the tidewater section of the State. From my own knowledge pellagra is seldom seen in those counties bordering on the Atlantic Ocean. This is not due to any lack of vigilance or knowledge on the part of the profession. All people in North Carolina are well acquainted with pellagra and if the doctor is tardy with the diagnosis the patient or the patient's friends make the diagnosis and hurry the sufferer off to some one in the nearest city who has had some experience with the disease. My office boy, a negro of no more than average intelligence, readily makes the correct diagnosis.

It is further noted that the death rate in the mountains of the western section of the State is almost nil. From an intimate personal knowledge of this mountainous section, I know that the disease here is practically unknown, and I have never found any knowledge of the conditions among the mountain people themselves.

The remarkable prevalence of the disease in the Piedmont section of North Carolina must be more than coincidental. It is well recognized that the mill towns of the State are peculiarly susceptible


Pellagra Deaths In
North Carolina Towns Of
Over 1000 Population, in 1911.
Legend
White Male
White Female
Colored Male
Colored Female
Summary
White Male 87
White Female 86
Colored Male 9
Colored Female 54
Total 176
Mount Airy 31
Reidsville 50
Oxford 32
Henderson 87
Elizabeth City 25
Edenton 36
Winston Salem 13
High Point 30
Greensboro 50
Chapel Hill 260
Durham 49
Rocky Mount 12
Plymouth 21
Lenoir 23
Morganton 72
Statesville 65
Salisbury 124
Raleigh 172
Wilson 25
Washington 40
Asheville 18
Concord 45
Hendersonville 103
Gastonia 37
King's Mountain 43
Charlotte 56
Goldsboro 62
New Bern 20
Fayetteville 62
Monroe 47
Wadesboro 41
Rockingham 135
Wilmington 94

to the disease, but it is also a notable fact that the cotton mill villages in the eastern counties are relatively free from the disease. For example, the village of Delgado, just outside of the city of Wilmington, with an estimated population of 1,000, and with a community made up of people very largely from the inland counties, has largely escaped the disease, and almost in every instance when a case has occurred it could be shown to have recently come from the up-country or to have spent several months of the year in their old homes.

In North Carolina it is a notable fact that many more cases occur on the streams and rivers of the Piedmont section than elsewhere.

The fact remains unexplained that there are many sporadic cases of pellagra among the aged when it is shown that the victim has long been bedridden or has not left the home for a long period of years.

PELLAGRA IN TEXAS; SOME SUGGESTIONS AS TO ETIOLOGY.

By K. H. BEALL, M. S., M. D., Member of the State Board of Health of Texas, Fort Worth, Texas.

Texas, like many of her sister States, faces this new health problem, and in the darkness of our ignorance as to the etiology of pellagra, there has arisen a conservative alarm. A disease which five years ago was of purely academic interest to our physicians, last year killed two hundred and seventy-six of our citizens, and invalided several thousand more.

The first report of a death from pellagra in Texas was made in 1907, and to August 1st of this year there had been reported four hundred and forty-three deaths from this cause. It is likely, but insusceptible of proof, that the disease existed in Texas before 1907, and it is, of course, true that no small part of the great apparent increase in the reported mortality from this disease is due to the education of the profession along this line. However, there can be no doubt that pellagra has increased greatly in the last few years, and that it is still very prevalent. No exact figures can be given as to the pellagra morbidity, but I am convinced that five thousand people in Texas are victims of the pellagra poison.

I have here a chart which shows the reported deaths by months. In this the usual summer increment is to be seen at a glance, likewise the increase in the number of deaths of the succeeding over the preceding year. I have not charted the mortality of the current year, but a comparison is gratifying in that there has been but little increase over last year.

Texas is a big State and has within her confines the greatest diversity of climate, soil, and altitude, and it is interesting to investigate the extent of the disease in different regions. Upon this map are charted the pellagra deaths reported to August 1, 1912. At the first glance there appears a pellagra belt through the eastern central portion of the State, but this is the populous belt and seven deaths in Jones county are, according to the population, about eight times as many as the nineteen deaths in my home county, Tarrant. This populous belt is the best watered part of the State, but I want to emphasize that, considering the population, it does not show the

heaviest infection, as, for instance, Jones county, referred to above, is not a well watered county, but when its population is considered, its mortality is very heavy.

To secure some evidence as to the probability of this disease being transmitted by some water-bred insect, as has been advanced by Sambon and accepted by many as likely, I have ascertained the proximity to water of the homes of fifty-four Texas pellagrins. Of these, but four lived near a stream, or less than one-fourth of a mile; nine lived from one-fourth to one-half of a mile; forty-one at least one mile; two lived eight miles; four ten miles; one, fifty miles, and one lived sixty miles from any lake or stream; a general average of over four miles. These figures argue only for probabilities, but cases like one which I shall detail argue strongly against the possibility of any water-bred organism being a factor. This was the case which lived fifty miles from any open collection of water, and investigation has shown that this woman had remained constantly at home for four years before the onset of the disease, all the time being in perfect health. These are facts, and we must either admit an incubation period of over four years in this case or agree that a water-bred insect was not a factor. Surely the first impression which the pellagra student would have on a visit to western Texas would be that "water-bred insects can here be eliminated," and had Sambon's expedition gone out to Texas instead of to Italy, especially during the last three years of drought, we should now be little concerned with the distribution of *Simulium*.

An interesting comparison may be made of El Paso and Navarro counties. The population of El Paso is greater than that of Navarro, but there have been eight times as many deaths in Navarro as in El Paso. El Paso county has a river, one of the largest of the State, and many irrigation ditches, so that water, or the lack of it, cannot make the difference. There are several factors to be considered—the greater altitude of El Paso county, the greater urban population and the smaller number of negroes.

In Texas, as elsewhere, pellagra is chiefly a rural disease, though cases in cities are by no means rare. It is more prevalent among the poor and those who live under bad hygienic circumstances, but often does it attack the refined and the affluent. The writer has seen three cultured physicians and three physicians' wives who were victims of this disease. Judging from the mortality reports and

from personal expérience, the disease shows an uncommon infrequency among children, for out of the four hundred and forty-three deaths which have been reported only fifteen were under fifteen years of age, less than 3½%.

Pellagra is prevalent among the negroes, but for many reasons no comparative statements can be made as to its prevalence.

I wish now to direct your attention to some startling findings which have come from a detailed study of four hundred and twenty-three deaths which have been reported to the Health Department, and, to make it easy for you to follow me, I have prepared a chart upon which may be seen the number of deaths as they occurred by decades of life in the two sexes. As I have stated above, the cases in children are uncommonly few, and, curiously indeed, the number of deaths for the first two decades are exactly the same in the two sexes. In the third decade, or from 20 to 30, the number of males has fallen, while the number of females (an astonishing thing!) has risen to sixty-one; in the next decade a further rise to eighty-two; in the next (40 to 50) to the high figure of ninety-one, while the number of deaths in males has kept a fairly constant level. In the next decade (50 to 60) the number of females drops to forty-five, while it appears that this decade is the most fatal one for males, the male curve reaching its maximum. In the next decade the male and female curves meet and continue together to the end of life. If we collect together the deaths of the three decades, from twenty to fifty, we find there are two hundred and thirty-four females and forty males, a ratio almost six to one. Now, if we *knew* the causes of pellagra we *could* explain the remarkable rise of the female curve; so, perhaps, if we *try* to explain this phenomenon, we shall get a little nearer to the solution of the enigma.

These figures indicate that in Texas females of a certain age are more susceptible to pellagra than are males, or when attacked, are less resistant to its ravages, or that they are more exposed. As to susceptibility, medical experience has not shown that females of twenty to fifty are more often attacked by any disease common to both sexes, except those due to disturbances of the thyroid gland. Shall we haul the thyroid gland into court to explain this greater incidence among females? I think not, though I confess that the nervousness, weakness, loss of weight, tachycardia, pigmentary

changes, diarrhœa, and eye phenomena often seen in pellagrins are suspicious symptoms, and I am also sure that the thyroid gland should be more carefully studied in these cases.

Are females less resistant than males? I do not think so, and while I cannot produce figures, I believe that the morbidity and mortality curves are a parallel.

So, denying them to be more susceptible or less resistant, I am forced to believe that women are more exposed to the causative agents than are males. Some interesting facts are these: there were more male deaths in the sixth decade from pellagra than in three decades combined, from twenty to fifty; in other words, there is a comparative immunity among males of the age at which the time spent in the home is the least. The average age of the female was thirty-nine; of the males forty-nine; a difference of ten years.

These observations have led me near to a conviction that one etiological factor in pellagra is something or condition or occupation in the home or around the house, for in no other way can I explain the greater number of cases in females and in those males, who, because of their age, spend most of the time at home. In Italy, where women share, to a greater extent, the labor of the fields, the number of cases among females, while still greater than that among males, by no means shows such preponderance as exists here, and surely the reason for such a great difference in incidence among females in Italy and Texas must be sought, not in a changed character of the disease, but in the different habits of the people. I am going to suggest, with great trepidation, however, that the agent may be active in the daytime only, for were it not so, those who spend little of the daytime at home, but most of the night, would not show such apparent immunity as seems to exist.

PELLAGRA IN THE CANAL ZONE.

By W. E. DEEKS, M. A., M. D., Ancon Hospital, Canal Zone.

In the Medical Record of March 23d, 1912, the writer published a report on twelve cases of "Pellagra in the Canal Zone." In it was stated the opinion that pellagra was due to an auto-intoxication, the result of carbohydrate fermentation in which corn may or may not enter as a factor.

Based on this etiology the cases treated responded promptly and the results in comparison to other methods in vogue were sufficiently satisfactory to justify their continuance.

Since the publication of this report, which covered the cases to November 1st, 1911, eighteen other cases have been admitted to Ancon Hospital, and of these a brief report is here presented with the results obtained when the same line of treatment has been faithfully carried out.

Of the former cases reported, one black female has re-entered the hospital with no symptoms of pellagra, but with pulmonary tuberculosis. Another case (the white man reported, Case 12) returned with some recurrence of his nephritis and stomach trouble following a relapse in his diet. The second warning has proved efficacious, however, and a recent examination shows that he is apparently in perfect health.

The other cases reported have not been readmitted.

In order to make this report as complete as possible the former cases published will again be briefly epitomized along with the more recent cases.

Case I.—J. W. O., Martiniquan woman, colored, 36 years of age; was admitted to Ancon Hospital June 16, 1910, with acute pellagra. The dermatitis was characteristic on the hands, forearms, and shins, also the mucous membrane of the mouth, rectum, and vagina. She complained of pain in the stomach, also on urination, and was sensitive to pressure over the abdomen. There was a sero-sanguinolent discharge from the vagina. The parts about the rectum were excoriated. The leucocytes were 10,400 with 65 per cent. polynuclears, 1 per cent. large mononuclears, and 18 per cent. lymphocytes. On admission the temperature was 100°; pulse, 128, and respirations, 24. The temperature and toxic conditions increased daily, and

she died on the 21st, five days after admission, with a temperature of 107°. Post-mortem: There were found an acute and subacute spinal meningitis, chronic interstitial nephritis, and chronic cholecystitis.

Case II.—L. D., Martiniquan, colored, male, age 40; four and one-half years on the Isthmus; was admitted July 13, 1910, complaining of having been sick for eight days, and unable to work because of pain in the joints and extremities. On admission the temperature was 110.4°; pulse, 128, and respirations, 54. Patellar reflexes absent; Romberg's sign present; gait, ataxic; unable to co-ordinate. He had the characteristic oral mucous membranes, but no dermatitis. From the midday of his admission he vomited almost constantly, was nervous, slept badly, and developed an uncontrollable diarrhœa; temperature increased, and he died on the fourteenth day after his admission with a temperature of 106°. His leucocyte count on admission was 11,200; polynuclears, 81 per cent.; large mononuclears, 4 per cent., and small mononuclears, 15 per cent. Post-mortem findings: Acute and chronic ulcerative colitis, proctitis, lymphadenitis (mesenteric and mescolic), chronic degenerative myocarditis, acute degenerative nephritis, and edema of the lung.

Case III.—V. C., female, colored, age 40, from Guadeloupe; was admitted to the hospital June 4, 1911, from Gorgona. She had been three months on the Isthmus. On admission she complained of having been ill twelve days with fever, vomiting, diarrhœa, and pain in the back. She had the typical dermatitis on the hands, forearms, and breasts, the red hyperemia of the oral mucous membranes, doughy abdominal skin, vaginitis, and proctitis, with excoriated skin about the perineum. In the vaginal discharges were gonococci. The leucocyte count was 13,000; temperature on admission 100°; pulse, 120; respirations, 36. She died on the fifth day after admission with a temperature of 106.5°. The autopsy showed multiple infraction of the kidneys and spleen, chronic nephritis, acute capillary bronchitis, acute splenitis, chronic adhesive peritonitis, syphilitic cirrhosis, mycarditis, and ulcerative stomatitis, and a general septicemia of undetermined origin.

Case IV.—S. U., colored, female, Martiniquan; local residence, Culebra; five years on the Isthmus. Was in the Ancon Asylum suffering from paranoid dementia præcox from June 26, 1909, to

September 13, 1910. She was discharged at the request of her husband, and was readmitted July 25, 1911, to the medical wards with a temperature of 100.4°; pulse, 128; respirations, 24. Her condition on admission was very critical, almost comatose. The dermatitis on the hands, forearms, and feet was very characteristic, also the acute inflammatory condition of the oral, vaginal, and rectal mucous membranes, with excoriated perineum and inner surfaces of the thighs. Her stools contained the ova of uncinaria and ascaris, with plenty of blood and pus. The urine contained a few hyaline casts; hemoglobin, 90 per cent., and leucocytes, 9,400. There was no diarrhœa. At this time, being impressed with the similarity of the early symptoms of pellagra, and those of patients who were large consumers of cane sugar and starchy foods, to the exclusion of meats, green vegetables, and fruits, the writer decided to use a special diet in which sugars and starches were absolutely excluded. The patient was given a diet of orange juice, milk, meat broth, and eggs, and the only medication was dilute nitric acid, 20 to 30 drops, three times daily in one-half glass of water on an empty stomach. An occasional dose of castor oil was also administered. Improvement in her physical condition was marked after the first two or three days, and in three weeks the dermatitis had practically disappeared, leaving a clear skin with only slight pigmentation. All the mucous membranes became perfectly normal, and physically the patient could be considered well. As her strength returned her mental symptoms became worse, and on the 22d of August, about a month after admission, she was transferred to the asylum in a maniacal condition. She died September 3d, twelve days later, and post-mortem findings revealed only a slight diffuse nephritis with a moderate acute degenerative process superadded, and a slight chronic ulcerative metritis, not enough to account for her death.

Case V.—G. P., Martiniquan, female, colored, age 27, six months on the Isthmus; was admitted August 22, 1911, with a temperature of 103°; pulse, 120; respirations, 32. Her physical examination was negative except for the characteristic stomatitis, vaginitis, and proctitis. She also suffered from pains in the lower extremities and abdomen. There was no dermatitis. Her leucocytes were 17,200. After three weeks of treatment she was discharged practically well.

Case VI.—M. D., female, colored, age 33, a native of Trinidad; was admitted from Gorgona on August 23, 1911, with a history of about one month's illness. She complained of some fever, abdominal pain, sore mouth and throat, and more recently diarrhœa. She had the characteristic intense stomatitis with superadded white exudate, an intense vaginitis, some nephritis, and a diarrhœa with plenty of pus and blood in the stool. Her leucocyte count was 11,000. She was put on treatment, and was discharged well on October 21, 1911. She was on admission in a very critical condition, much prostrated, but was able to sit up and move about three weeks after admission.

Case VII.—J. G., Martiniquan laborer, colored, age 26; had been on the Isthmus six years; was admitted to the hospital on September 27, 1911, complaining of swollen legs and arms, and sore mouth. He had the characteristic dermatitis of the forearms and hands, and the sore mouth. Otherwise the physical examination, including the stools and urine, was negative. He was placed on treatment, and discharged well on October 15.

Case VIII.—H. W., female, colored, Jamaican, age 25, who had been several years resident on the Isthmus, was admitted from Paraiso on September 16 with a temperature of 102.5°; pulse, 120; respirations, 26. In this case the dermatitis was very marked on the dorsum of the hands, wrists, and forearms. There were the usual mouth and vaginal symptoms characteristic of the affection, but no diarrhœa. She improved rapidly under treatment and was discharged November 11.

Case IX.—I. H., female, Jamaican, colored, age 35, with a history of eight years' residence on the Isthmus; was admitted September 24, 1911, suffering from diarrhœa of 15 days' standing. The oral and vaginal mucous membranes were in a highly inflamed, irritable, red condition, and the dermatitis, which extended up to and included the elbows of the upper extremities and the dorsal surfaces of both feet and toes, was very characteristic. Blood examination showed 75 per cent. of hemoglobin, 3,640,000 reds, and 4,800 whites. Stool examination showed blood and pus, and urine showed pus, albumin, hyaline, and granular casts. Her condition was very grave; temperature 99°; pulse, 110, and respirations, 20. Under treatment she began to improve, and by the middle of October she was able to be up and around. She was discharged well on the

22d of October. The mental symptoms characteristic of the later stages of the disease were present only in showing extreme irritability.

Case X.—H. W. B., Jamaican, female, colored, age 27; arrived on the Isthmus when a child; was admitted October 26, 1911, complaining for seven days of fever at night, sore mouth, with extreme salivation, constant pains in the abdomen, frequent watery bowel movements, occasionally with blood. The oral, vaginal, and anal mucous membranes were exceedingly red and irritable, with the abdominal pain distressing. There was a patch of dermatitis on the right side of the abdomen about the size of the palm of the hand, but none on the extremities. Her stools showed misroscopically pus cells, her urine a slight trace of albumin, hyaline, and granular casts. Her blood showed 2,624,000 red cells, 21,600 whites, with 80 per cent. polynuclears, 17 per cent. small mononuclears, and 3 per cent. large mononuclears cells. Her mouth and vaginal mucous membranes recovered very quickly, and in four days the irritable condition was almost gone. Her abdominal condition persisted, and was very much worse for one week after treatment was begun. Her face had the drawn expression of a fatal peritonitis. The use of saline enemata, however, with bismuth subnitrate by mouth relieved this, and convalescence rapidly ensued. She was discharged well on November 21, 1911.

Case XI.—M. M., female, Barbadian, age 29, three years on the Isthmus; was admitted to the surgical side October 30, 1911, complaining of nausea, vomiting for the past two months, with some vertigo and numbness of the legs of two days' duration. She had some chronic pelvic peritonitis, for which an operation was performed. On November 13, two weeks after admission, my attention was directed to her because of the peculiar condition of her tongue. On examination she was found to have not only the characteristic tongue, but also the vagina, and the doughy, inelastic skin, with patches of pigmentation about the elbows. The case was not a very severe one, and on treatment she rapidly recovered. The symptoms she complained of on admission were more or less typical of pellagra patients. She was discharged on November 26.

Case XII.—W. J. M., white, American, born in Indiana, age 34, a conductor who had been four years on the Isthmus; was admitted to the hospital November 1, complaining of having been for

two days ill with chilly sensation, slight fever, headache, nausea, vomiting, insomnia, sore throat, and burning in the stomach. The upper extremities and neck were affected by a severe dermatitis, which he said had existed for two weeks and was caused by sunburn. The dermatitis extended to above the middle of the arms, corresponding precisely to the parts uncovered by his undershirt. He wore elastic sleeve holders above his elbows, and the part protected by them was free from dermatitis, thus proving beyond question that the dermatitis is excited at times by the sun's rays. His tongue was so irritable, red, and inflamed that he could not protrude it. The buccal mucous membrane was in a similar condition with ulcerated lesions on the lower lip, and constant salivation was present. The skin was so doughy that when a fold was caught up it remained in that condition for some time. He had an associated very severe acute nephritis, with a large amount of albumin, hyaline, granular and epithelial casts, and was passing from 11 to 20 ounces of urine daily. Nausea and vomiting were almost constant, and insomnia from the distress and burning in his stomach. His blood examination showed a leucocytosis of 17,000, and a differential of 86.5 per cent. polynuclears, 4 per cent. small mononuclears, 6.5 per cent. large mononuclears, and 3 per cent. transitionals. For two days after admission he had to be kept under the influence of morphine, and his life was despaired of. For four days only liquid could be retained. Convalescence then began and progressed rapidly. The oral symptoms first cleared up, and the stomach distress disappeared. Three weeks after admission his only complaints were of dull rheumatic pains in his legs and hips. He was discharged November 29 well, except for occasional hyaline and granular casts in his urine. The albumin had entirely disappeared. No case could be more typical of severe pellagra than this, though he had not reached the stage where diarrhœa and mental symptoms appear.

Case XIII.—M. W., colored, female, from Montserrat; local residence, Panama; three years on the Isthmus; was admitted to the surgical ward May 24, 1912, with vaginitis and peniritis of external genitals; discharged at her own request. She was readmitted June 10, 1912, with mental symptoms of hallucinations of sight and hearing and transferred to the asylum. She was anæmic, weak and had intense apathy and listnessness. The temperature varied from 98° to 102°. The oral, rectal and vaginal mucous membranes were

irritably red and inflamed. The urine contained a slight trace of albumin, but no casts; also a high trace of indican. Hæmoglobin, 40 per cent. There was dermatitis about both wrists and ulcerations on the labia majora. Stool negative, also Wasserman. The patient died July 8th, and autopsy showed an acute ulcerative and exudative stomatitis, glossitis, tonsillitis, pharyngitis, œsophagitis, proctitis, vaginitis, dermatitis, simusitis, and lymphademitis. There was also complete transition of all the adbominal and thoracic viscera, an atrophic heart with some pericardial effusion.

Case XIV.—L., colored, female, Martiniquan; was admitted to the Asylum June 13, 1912, wildly delirious and with an alcoholic history; no history otherwise obtainable. Three months after her admission a symmetrical dermatitis was observed beginning in the elbows and anterior surfaces of the wrists. The mental symptoms became aggravated. The oral, rectal, and vaginal mucous membranes were intensely red and inflamed, and diarrhœa developed. The temperature ranged from 98° to 100°, the urine showed albumin and casts, both hyaline and granular. Treatment was instituted, and she is now convalescent physically and mentally.

Case XV.—E. W., colored, Jamaican, female, age 40; was admitted to the Asylum July 26, 1912, in a confused and apathetic state. She had convulsions previous to admission, but no other history obtainable. On admission temperature was 100°; pulse, 126, and respirations, 30. She answered questions slowly and reluctantly, and had delusions and hallucinations. Her oral, rectal, and vaginal mucous membranes were intensely red and inflamed and she swallowed with great difficulty. Her urine showed numerous casts, hyaline and granular and no indican. She developed an acute pulmonary condition and died August 11th. The autopsy showed acute purulent bronchitis of both lower lobes with small areas of broncho-pneumonia, chronic nephritis and cloudy swelling of kidneys, heart and liver; chronic ulcerative enteritis, chronic lymphadenitis, pyorrhœa alveolaris, atrophic glossitis, chronic urethritis and cervicitis; atrophic heart, spleen and liver; and pigmented exfoliative dermatitis of the wrists and elbows.

Case XVI.—F. J., colored, male, Martiniquan; was admitted December 19, 1911. His illness dates back one month when he suffered from pain in the epigastrium with vomiting. On admission the temperature was 101°; pulse, 76; respirations, 28. The oral

examination showed the tongue and buccal mucous mebrane intensely red and inflamed with patches of white membrane superimposed. There was pus and blood in the fæcal discharges. Marked tenderness was present over the abdomen. There was inelastic skin and pigmentation on the lower extremities. The urine showed the presence of albumin, hyaline and granular casts.

Under our routine treatment he recovered and was discharged January 11th. Before his discharge, three successive examinations of the urine were completely negative.

Case XVII.—L. A., colored, male, age 50, from Guadaloupe; four years on the Isthmus; was admitted December 23, 1911, with a history of one week's illness, complaining of abdominal pains and gaseous eructations.

His tongue and oral cavity were typically pellagrous. The dorsi of both hands were covered with acute dermatitis; the skin inelastic and evidence of myocarditis and marked arterio-sclerosis. He left the hospital free from pellagra symptoms in three weeks.

Case XVIII.—A. G., colored, male, Barbadian, age 22 years; four months on the Isthmus; was admitted January 16, 1912, with a history of ten days' illness. On admission temperature was 99°; pulse, 100, and respirations, 24.

The tongue was red and irritable, and a marked dermatitis on the forearms and dorsi of the hands was present. His physical examination was otherwise negative. On the usual routine treatment he rapidly cleared up and was discharged on January 29th.

Case XIX.—J. W., colored, male, Barbadian, four years on the Isthmus; was admitted on May 30th with a history of three weeks' illness, which began with hiccough and vomiting. On admission his temperature was 100.5°; pulse, 114, and respirations, 22. The tongue and buccal cavity showed the intensely red character with superficial ulceration. Diarrhœa was present and nephritis with a large amount of albumin and numerous hyaline and granular casts. There was no dermatitis. He was discharged June 20th, after routine treatment, absolutely well except for a few hyaline casts in the urine.

Case XX.—E. V., colored, female, Martiniquan, age 32, who had been five years on the Isthmus; was admitted January 29, 1912, in semi-comatose condition; no history obtainable. There was the red irritable tongue and ulcerative stomatitis with acute vaginitis

and dermatitis of the exterior surfaces, the hands and wrists. She died twelve hours after admission and no autopsy was performed.

Case XXI.—E. D., colored, Martiniquan, female, age 40; 25 years residence on the Isthmus; was admitted to the hospital February 13, 1912, with a history of dysentery for five months. The tongue was red and irritable with salivation. She was anæmic; had acute vaginitis with labial excoriation; nephritis with albumin, hyaline and granular casts, and dermatitis of both hands and wrists and inelastic skin. On routine treatment she repaidly recovered, and was discharged March 2d. A few casts still remained in the urine.

Case XXII.—L. A., colored, male, St. Lucian, age 42; 24 years on the Isthmus; was admitted May 23, 1912, with a history of three months' illness, beginning with an eruption on the back of the hands, diarrhœa and insomnia. His tongue and buccal cavity were typically inflamed, the dermatitis on the hands characteristic and some nephritis with the urine showing albumin and casts was present. Under routine treatment, he rapidly convalesced and was discharged well on June 18th. The urine was negative before his discharge.

Case XXIII.—D. J., colored, male, St. Lucian, 27 years on the Isthmus; was admitted July 5, 1912, with temperature of 99°; pulse, 100, and respirations, 26. He was semi-comatose and had a history of six days' illness. He had the oral symptoms, marked dermatitis of hands and feet and face; constant hiccough, and died the next day. His autopsy showed atrophic glossitis, pyorrhœa, alveolaris, a few small areas of fatty liver metamorphosis and atrophic spleen. There was no organic tissue sufficient to account for his death, except the toxic condition of acute pellagra.

Case XXIV.—C. S., colored, Jamaican, female, age 20; four years on the Isthmus; was admitted December 11, 1911, with a history of four months' illness. On admission the temperature was 100°; pulse, 110, and respirations, 24. The tongue and buccal cavity were red and ulcerated and marked dermatitis on the dorsi of hands and wrists was present. The urine was negative. She was discharged January 7th very much improved, but her pulse was still rapid.

Case XXV.—M. M., colored, Barbadian, female, age 28; three and a half years on the Isthmus; was admitted December 15, 1911. One month previously had been operated on for pelvic peritonitis.

Now has developed epigastric pain, dermatitis on the dorsal surfaces of both feet and toes, and has the oral inflammatory condition. She rapidly improved and was discharged well on December 28, 1911.

Case XXVI.—H. N., colored, male, from Guadeloupe, age 40; admitted August 20, 1912, complaining of trouble with hands and feet of fifteen days' duration. He had estivo-autumnal malaria and a very severe nephritis. His tongue was heavily coated, but not typically pellagrous. He complained of abdominal pain and died two weeks after admission.

The pathological report was as follows: nephritis, chronic diffuse, extensive, with acute, diffuse degenerative superimposed atheroma of mitral leaflets with cardiac hypertrophy and dilatation; fatty metamorphosis of the liver and congestion of the colon mucosa.

Case XXVII.—D. H., colored, Barbadian, male, age 39; was admitted August 9, 1912, with a history of four days' illness. He was suffering from severe dysenteric symptoms, but had no fever. Physical examination showed the red, irritable tongue and buccal mucous membrane. Acute dermatitis was present in the dorsi of both hands, also about the elbows. There were ulcerations in the rectum and plenty of pus, blood and ciliated monads in the stools. The urine was negative, also the examination of other organs. The patient was placed on the usual treatment and though still in the hospital, has made a perfect recovery, September 12th.

Case XXVIII.—J. B., colored, Martiniquan, male, age 33; was admitted August 20, 1912, with a history of headache, fever and vomiting of four days' duration. He was emaciated and weak, had a red, irritable tongue with white patches, also a similar buccal mucous membrane and fissures in the corners of his mouth. His skin was doughy and inelastic and he had a small patch of typical dermatitis which gradually increased in extent on the dorsum of one hand. This gradually extended to the other and crept around on the palms. There was also acute eczema on his forehead and about the nose and corners of the mouth. Diarrhœa also was present and nephritis of mild grade. The membrane on the mouth was negative for Vincent's Angina when examined bacteriologically. Proctitis was present with severe excoriations about the arms.

The patient later also developed mental symptoms, was apathetic and mildly delirious. On treatment the patient has greatly

improved. The mouth condition is now normal, the dermatitis has subsided and the mental and gastro-intestinal symptoms cleared up.

He is still in the hospital with some eczema and nephritis persisting.

Case XXIX.—A. H., colored, Jamaica, female, aged 27 years, has been six months on the Isthmus; was admitted July 8th, complaining of nausea and vomiting of two weeks' duration. Physical examination showed the usual severe, red, irritable, superficially ulcerated tongue and buccal mucous membrane with consequent painful mastication, drooling and inability to open the mouth and protrude the tongue. There was epigastric tenderness, also severe diarrhœa.

Acute vaginitis was present and four months gravid uterus. The urine showed albumin, hyaline and granular casts of severe grade. Skin inelastic, but no evidence of dermatitis. Mentally she was at times melancholic. The patient soon aborted, but upon treatment made a good recovery and was discharged well on August 20th.

Case XXX.—E. W., colored, female, was admitted August 31, 1912, with a history of six weeks' illness with fever, vomiting, constipation and progressive loss of weight. Physical examination showed unusually severe oral mucous membrane inflammation with white patchy exudate, marked salivation, great difficulty in talking and swallowing, and inability to masticate food. There was epigastric pain and abdominal tympanitis. The urine showed albumin, hyaline, and granular casts. Vaginitis moderately severe was present. There was the usual inelastic skin, but dermatitis only about the elbows.

The patient has made an excellent recovery, but is still in the hospital on September 15th.

As pointed out in my previous publication, the symptoms can be briefly described under six heads, as follows: oral, gastro-intestinal, genital, dermal, nephritis, and mental. In this connection I would like to draw the attention to the pathological lesions found in Case 13 of this series, in whom all the symptoms referred to were present to a marked degree and were confirmed at autopsy.

This was an asylum case, had a history of insanity a few years previously and had been in the hospital a few days before the mental symptoms developed with a vaginitis and pruiritus. It has been my experience that when mental symptoms develop, which are late

manifestations of the disease, the chances of recovery are very much lessened, even though the physical symptoms disappear.

I have adopted the above system of classification of the symptoms because of the clinical advantages and not because of its being anatomically or physiologically scientific.

These clinical manifestations can thus be briefly summarized:

Oral: The tongue is irritable looking, scarlet red in color, and protruded with difficulty, if at all. At times it is covered with a grayish, diphtheritic looking membrane on the edges, and sometimes the dorsum. The mucous membrane of the rest of the oral cavity is similar in appearance with superficial ulcers frequently present. There is profuse salivation and often fissures in the mouth corners. These appearances are very constant and were absent in only one of the thirty cases in my series. They varied only in degree of severity.

Gastro-intestinal: The symptoms referrable to the alimentary tract are several. The stomach symptoms are similar to those of an exaggerated hyperchlorhydria or nervous dyspepsia, heartburn, frequently intense, and associated with a similar chest pain due to œsophagitis. Nausea and vomiting are present generally and are frequently very severe. Food is craved, and when swallowed may be instantly rejected.

Diarrhoea often ensues and may be so severe as to play an important factor in the lethal termination. In these cases blood and pus are constantly present in the stools and acute ulcerative and exudative lesions are found post-morten throughout the whole intestinal tract.

Proctitis is very constant and is generally associated with excoriations about the anus due to the acrid discharges. Gastro-intestinal symptoms were present in twenty-three of the cases, or 77 per cent.

Genital: These symptoms are present in the female and are of the nature of an intense vaginitis with a thin irritating discharge which excoriates the surrounding parts. The mucous membrane has the same scarlet red appearance as referred to in the buccal cavity. This condition was present in sixteen of the nineteen females in the series, or 84 per cent.

Dermal: The dermatitis which is very characteristic of the disease was present in twenty-five of the cases, or 83 per cent. The most frequent positions were the dorsal surfaces of the hands and fore-

arms, but frequently also the neck, elbows, feet and about scar tissue. Occasionally a patch was met with on the body.

In a case previously reported it was shown how the clothing limited the lesion which on the exposed parts is undoubtedly the result of direct sunlight. Auto-inoculation, as Bass has shown by the nasal or oral secretions, may account for the more radial distribution on the forearms.

In addition to the dermatitis, the skin loses its elasticity, particularly when nephritis or ulcerative ileo-colitis is present. When a fold is caught up and released, it crawls more or less slowly back, instead of with the natural spring.

Nephritic: Evidence of nephritis of slight or moderate severity was present in twenty-five of the cases, or 83 per cent. Some showed chronic changes, others those of acute conditions which rapidly subsided on treatment. Three cases, however, were extremely severe and were responsible for two of the deaths in the series; the third one made a good recovery.

Mental Symptoms: These symptoms may be temporary and mild, or may become so grave as to necessitate asylum treatment. Of my series, four were asylum cases and of these, three died. The fourth is at present convalescent.

When severe mental symptoms develop the chances for recovery are greatly lessened. Eight of the cases showed mental symptoms of great irritability, hallucinations, confused ideas, or depressed state of mind, but rapidly recovered on treatment.

Results of the Treatment of the Series: Of the previous cases reported four of the twelve died, and of these four only one was treated by the present method in use here. That case cleared up from the physical symptoms, but died in the asylum from an exhaustive psychosis. Of the last eighteen cases, two died in the asylum from causes stated in the case reports (Cases 1 and 3). Two died within twenty-four hours of admission and cannot be considered as treated cases, and one died with nephritis. (See case Report No. 26.) The rest recovered, or are at present convalescent in the hospital. This makes a remarkably good showing and the results are usually obtained in from two to four weeks.

It is not my intention to discuss the various theories of the etiology of the disease, but to reiterate what I have already written on the subject—that the disease is the result of an auto-intoxication

caused by the action of some ferment or organism on a carbohydrate diet to excess, to the exclusion of green vegetables and fruits during the warm weather when metabolic activity is lessened. That is the hypothesis upon which my treatment is based and results obtained.

As may ideas in regard to the etiology and treatment have not mterially changed since my last paper was written, I will quote largely from that report.

From the above cases certain facts stand out prominently, and from these some conclusions can be drawn as to etiology. They are: (1) There is no endemic center. The patients were admitted from different localities on the Zone and came from different islands to the Zone. (2) Women were affected out of all proportion to the men, when the population here is considered. This is significant and will be referred to later on. (3) No race is exempt, but the disease seems to prevail among the poorer people, or those accustomed to live upon the cheaper or less nutritious foods. This leads to a consideration of the nature of these foods. Careful inquiry was made as to the diet in the above cases. Though it is very difficult to get anything like accurate information from the uneducated colored people, enough was gleaned to conclude that the usual corn diet which has been held responsible for the disease for years is only a subsidiary factor. When consumed largely it probably is an important factor, but when taken sparingly is no more of a factor than any other cereal or starchy food.

For some years my attention has specially been directed towards the influence of diet in disease, and the rule played by the different groups of food stuffs in the etiology of many affections. The information thus obtained when applied to a study of pellagra cases has been suggestive not only as to etiology, but also as to treatment.

In the "New York Medical Journal," June and July, 1904, the author published an article entitled "The Carbohydrates as Etiological Factors in Stomach Disorders," in which attention was drawn to the ingestion of cane sugar being responsible for practically all of the cases of so-called hyperchlorhydria or acid dyspepsia, and second, the consumption of the starchy group, including chiefly bread and potatoes to the exclusion of proteids and green stuffs, underlying that large group of so-called flatulent dyspepsias. These two types grade one into the other. About one year later, in the same journal, attention was drawn to the fact that acute rheumatism

and rheumatic manifestations followed the use of these same foods, the result of an auto-intoxication with, in acute cases, a superadded infection on the irritated tissues. In The Medical Record, October 8, 1912, another article was published on this same subject, entitled "The Carbohydrate Diathesis," in which it was advanced that not only stomach disorders and rheumatic affections were the result of this group of food stuffs, directly or indirectly, but many others, including nephritis. The similarity of the digestive troubles preceding the typical pellagrous manifestations to those of the carbohydrate group was so suggestive that a study of the diet as a whole was undertaken without the centralizing thought that corn must be held responsible, but that other food factors might contribute. This has been abundantly and strikingly confirmed. In some cases no history of the consumption of corn in any form could be obtained; in others only in great moderation. All, however, are consumers largely of sweet and starchy foods to the practical exclusion of proteids, green vegetables, and fresh fruits. In all, the sweet condensed milks of commerce, cane sugar, jams, rice, potatoes (Irish and sweet), and bread were the staples of their food, while meat or fish was consumed once or twice a week and vegetables and fruits sparingly, or not at all.

From an extensive experience here in the tropics it has been found by those of us who are interested in the subject of diet and its influence on disease that health is best maintained and much suffering avoided when sweet and starchy foods are excluded from the dietary or reduced to a minimum. There is no question that our metabolic activities here are less than in the North, corresponding to the lack of energy which is notorious in a warm, humid climate; and the proper digestion and assimilation of the carbohydrate group requires the highest degree of metabolic activity. When this does not take place fermentation or incomplete metabolism results, with the development of toxic products, which are absorbed into the system, thus causing a general auto-intoxication. That is the reason why pellagra always diminishes or disappears in the winter and lights up in the spring. That is the reason why women are more affected than men, because they do not do the same amount of physical work as men, their lives are more sedentary, and consequently their digestive functions are more sluggish.

The reason why pellagra is on the increase as shown by statistics are two: First, a better knowledge of the disease, and consequently more cases are reported. Second, and more important, because the consumption of sugar has increased inordinately in all civilized countries. For example, in England 300 per cent. per capita in fifty years. Last year the United States consumed 3,350,000 tons of sugar, or in a population of 90,000,000 almost 74½ pounds per capita, or 3.28 ounces daily. Provided, however, that only one-half of this amount is consumed, that is more than sufficient to set up the train of symptoms from which the American race now suffers. Taking into consideration that one-half the citizens do not consume one-quarter of this amount per capita, it can readily be seen to what extent some of the people have adopted the use of this form of chemical alcohol. There is nothing in the stomach to convert it into an assimilable product, consequently it is subject to the action of the bacteria of fermentation, which convert it into irritating, diffusible organic acids by taking up hydroxyl molecules, thus producing more of them by weight than the sugar ingested. These produce local irritations and subsequent toxemia. Starchy products act similarly, but in a milder degree, and produce more flatulence. The use of the much advertised cereal products has increased in like proportion to that of sugar.

I believe that it is not corn alone, but any cereal or starch food in conjunction with cane sugar, in a warm climate, where there is lessened metabolic activity, and consequent inadequate elaboration of digestive elements, which initiates the auto-intoxication responsible for the symptom-complex known as pellagra. The proof thereof lies not in the determination of the elusive complex physico-chemical substances, the result of fermentation or defective metabolic elaboration, but in the results obtained by physiological treatment based on the above mentioned hypothesis.

Treatment: This consists (1) in limiting the nourishment absolutely to fresh fruit juice, preferably orange, meat broths, and milk, as long as there is nausea or vomiting, and the absolute avoidance of everything which contains sweet or starchy elements; (2) in the administration of from 15 to 30 drops of dilute nitric acid in three-fourths of a tumbler of water three times daily on an empty stomach. I have found by practical experience that no drug known to me will relieve as quickly or as satisfactorily gastric acidity as

this mineral acid. When the stomach condition improves, which is generally in three or four days, a carbohydrate-free diet is ordered. This consists, in addition to the above, of eggs, meats of all kinds, fish, green vegetables, such as lettuce, celery, onions, tomatoes, beets, carrots, spinach, chayoti, vegetable marrow, okra, green peas, string beans, eggplant, etc., and fresh fruits of all kinds, there being no limitation. The nitric acid is continued three times daily before meals. Any other medication is but symptomatic, as indicated. The results obtained follow as quickly as do those from the treatment of gastric acidity in the same manner.

Recurrences: As yet I have had no experience with this, excepting the case referred to above in the American who relapsed in his diet, but I believe that the reason for recurrence in this affection is that hospital patients are necessarily restricted in their diet, and when recovery ensues they are discharged, not warned to avoid anything but corn and corn products, and they relapse to their former diet. If, however, they were told to avoid sugar in every form, cereals and an excess of starchy food, I do not believe that relapses would occur. It is interesting and exceedingly important in these cases to observe how rapidly the most severe acute nephritis clears up in this diet. The effects are just as rapid as those of a nephritis following scarlet fever or malaria. I have been so impressed with this fact that I now believe that almost all of our acute and chronic nephritic cases, the latter particularly of the interstitial type, other than those resulting from toxic acute infectious diseases, are due to an auto-intoxication, the result of the ingestion of sweet and starchy foods to excess. The results here obtained in treating these cases on the diet above suggested for pellagra cases have been astonishing. The increased vigor which follows in interstitial cases with the disappearance of the neuralgia, polyuria, and albumin, and the dimunition of casts, the hæmoglobin recovery, and the apparent restoration to health have been so striking that I am following this method now in the treatment of these cases.

In presenting this paper to the profession I do so in the hope that my results will encourage some others to try these simple measures, for I believe that therein lies the etiology and the treatment of pellagra.

PELLAGRA IN THE BAHAMAS.

Report of a Case Believed to Be Pellagra at Abaco, One of the Bahama Islands, By J. A. MACKINTOSH, M. D., Surgeon B. T. Co., D. M. O., Etc., Wilson City, Abaco, W. I.

As comparatively few people know much about the Bahamas, a few prefatory remarks may be forgiven.

The Bahamas form a chain of islands extending for about five hundred miles east and south of Florida. The group consists of some twenty inhabited islands and an immense number of islets and rocks, comprising an area of nearly 6,000 square miles. The islands are an unimportant colony of Great Britain. The population in 1911 was 56,000, the greatest part being descendants of liberated Africans. The chief industry is sponge gathering. The fruit trade with the United States up to a few years ago was of considerable importance. Enterprise is lacking to encourage industries.

The colony was at one time a hot-bed of yellow fever. It is recorded that shortly after the erection of Fort Charlotte near Nassau, almost the whole of the Forty-seventh Regiment, including men, women and children, was swept away by yellow fever in a few weeks. This was at the end of the 18th century. In 1802 the Seventh Fusiliers buried 226 of 366 men. In 1803 the fever again broke out and reduced the garrison from 300 to 50. These were saved by removal to another spot, but on their return the commanding officer and nearly every man died.

In recent years there seems to have been no yellow fever in the colony, which is probably due to good furtune, rather than to good management. The "Scots Grey" mosquito is much in evidence.

Leprosy is very common and while the census of 1911 gives only eighteen, this is far below the real number. More than that number of cases have been under my personal observation. It is prevalent in this island, Abaco. No segregation is practiced and no precautions are taken against the disease. The disease is confined mainly to the poor whites.

The majority of the colored population eke out a wretched hand to mouth existence, and live in defiance of all hygienic laws. Tuberculosis and venereal disease are rampant.

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Recently hookworm has been reported, at about the same time, in two different parts of the colony by two independent observers.

During six years' service in practically all parts of the colony, the writer has kept a constant watch for pellagra. The local conditions seem to be ideal for the disease from practically any of the supposed etiological factors. The principal foodstuff is hominy, much of it ground from native Indian corn. The majority of the population are very poor. Sand-flies are one of the pests of the country. Migratory birds are numerous and flies and mosquitoes more than plentiful.

The case here quoted is the first under observation that suggested pellagra (during the six years) and is apparently the first reported from this colony. The patient has seemingly disappeared, as all trace of him has been lost for about six months.

The patient, a man about 70, was born in the colony and has lived here all his life. He is native white in origin, married, and had seven children, only one living. Is in poor circumstances, occupation farmer-fisherman, a common means of livelihood here. He claims that neither parents, wife or children were ever afflicted with any similar disease. Onset, sudden, duration about fifteen years; began in about present location. He is thin, pale and somewhat emaciated, has a "peculiar staring look," complains of weakness, poor memory, giddiness, insomnia, persistent diarrhœa, failing vision, cramps in muscles of legs, numbness of feet and hands, is irritable, stupid and morose.

The eruption (?) involves the dorsum of both hands and both feet, with a few scattered patches on the forearms. The patches of erythema are irregular in outline and intensity. The skin about the ankles, wrists and in patches on the backs of the hands and feet, is dark brown. Affected areas are swollen and tense. The congestion disappears completely but temporarily on pressure. At times there is exfoliation. Sometimes, especially on exposure, blebs filled with clear serum form. No seasonal variation has been observed by the patient. Face and body are not involved.

His diet is mainly fish, hominy, sweet potatoes, conchs and wheat bread. He claims to have been a strong, healthy man before onset of disease. The natives think he has leprosy and avoid him.

The so-called pellagrous triad of erythema, nervous and digestive disturbances is here, and this with the other features led to the probable diagnosis of pellagra.

PELLAGRA IN PORTO RICO.

By GUIELLERMO CURBBELO WATERTTON, M. D., Superintendent, Insane Asylum, San Juan.

Pellagra is not a common disease in Porto Rico. I was appointed superintendent of this institution in November, 1907, and previous to that time I had never heard of any observations made on that disease. Upon my arrival here, after investigating and carefully studying on a case which I suspected to be pellagra, I diagnosed the case as such. Since that year we have had two more cases. These are probably the only cases of pellagra that have been observed in this country, with the exception of one case observed in the municipal hospital here.

NOTE.—B. K. Ashford has reported one case of pellagra in Porto Rico. These brief notes serve to establish the presence of pellagra in the island.

PELLAGROUS INSANITY IN EGYPT.

By DR. R. W. J. PEARSON, L. R. C. P., L. R. C. S., Ed. Sub-Director of the Government Hospital for the Insane, Abbassia, Cairo, Egypt.

Pellagra as a cause of insanity in Egypt attracted little notice until the year 1895. In this year Dr. Sandwith drew the attention of Dr. Warnock to the prevalence of this disease, with the result, that Dr. Warnock, in his annual report for 1896, mentions pellagra as the cause of 11 cases of insanity.

The following table shows the pellagrous admissions at Abbassia Asylum from 1896 to 1911 inclusive:

ANNUAL ADMISSIONS OF CASES OF PELLAGROUS INSANITY.

Year.	Males.	Females.	Total.
1896	9	2	11
1897	13	10	23
1898	29	10	39
1899	14	19	33
1900	27	8	35
1901	23	10	33
1902	22	9	31
1903	41	11	52
1904	38	15	53
1905	54	11	65
1906	91	33	124
1907	69	20	89
1908	71	17	88
1909	68	33	101
1910	74	35	109
1911	81	26	107

It will be seen from the above figures how serious a cause of insanity pellagra is in Egypt. The cause of the rapid increase in the number of pellagrous cases in late years is due to the more careful examination for pellagrous symptoms. The above table refers to cases of insanity due to pellagra; not to cases showing symptoms of pellagra on admission, whose insanity is due to other causes than pellagra. Large numbers of patients are admitted to the asylum whose insanity is due to other causes, such as epilepsy,

adolescent dementia, etc., but who show signs of pellagra on admission. These are not classed as pellagrous insanity, but come under other diagnoses.

In his annual report for 1907, Dr. Warnock mentions, that pellagra was the cause of 576 cases of insanity in the preceding eleven years, while numbers of other cases (which were admitted) had symptoms of pellagra. In the year 1909 the total number of admissions was 578. Of these 101 were cases of pellagrous insanity. In 1910 and 1911 the total admissions were 721 and 778, of whom 109 and 107 were cases of pellagrous insanity.

It may be roughly stated that the proportion of females to males is as one to three. Almost all the cases of pellagrous insanity come from the country districts and the small villages. They are nearly all of the fellaheen (agricultural) class. A few cases come from the large towns, but these on being questioned state that they have been in the towns for a short time only, having come in search of work from the country districts. They nearly always state that maize has been their staple article of diet and many of them say that they have used inferior and decayed maize.

Most of our pellagrous cases come from the Delta, where maize is extensively grown and eaten. Fewer cases come from upper Egypt, where millet is more used than maize, and practically none from the Soudan, where a great deal of millet and practically no maize is grown at present.

Dr. Warnock has observed that pellagra is common amongst children in the Delta. He has seen numbers of children of the ages from 10 to 15 years, dwarfed, cachectic, anemic, and having distinct black pellagrous rashes. Some of these children were insane. On admission to the asylum almost every case of pellagrous insanity is found to be suffering from Bilharzia, or ankylostoma or some other parasite; the greater number being on the scalp Many of them are almost completely bald from this disease.

In fact the pellagrin seems to be a home for parasites of all descriptions, this condition being probably due to his lowered vitality.

The physical symptoms as observed here, in addition to the cachexia, anemia, and extreme exhaustion usual in these cases, are the customary black rash on the face, neck, forearms, hands, feet and legs. The rash is also seen wherever there is pressure, such

as at the girdle, over the trochanters, on the knees, elbows, etc., and there is generally thickening of the soles of the feet.

It may be stated that the rash appears wherever there is exposure to the sun and weather, and also where there is pressure on the skin. In all of our cases the parotids are markedly enlarged, the tongue is denuded, there are always digestive troubles, and a distinct dilatation of the stomach. I am inclined to think that the enlargement of the parotids is a compensatory hypertrophy to produce more saliva in order to neutralize the excess of acid in the stomach which is commonly present in these cases.

Pellagra in this country affects the sebaceous glands of the nose and the cheeks, causing a hypertrophy of these glands. The glands become chock full of sebaceous matter, giving to the patient a distinctive, mottled appearance. The main incidence of the rash here is in spring and early summer, rarely in autumn. Dr. Warnock has observed that the rash and diarrhœa occur simultaneously, and has inferred from this that the rash is not a casual symptom, produced by the exposure of a pellagrous person to the sun's rays, but is a sign of a general morbid process affecting the whole organism.

The mental symptoms are usually of the melancholic type, but there are occasional cases of mania which sometimes become furious. The patients complain of burning sensations in the mouth, stomach and intestines, and of excessive thirst. They also complain of painful points and burning sensations over the spine. For the latter as well as for the gastric and intestinal symptoms, they are freely cauterized by the village barbers before their admission to the asylum. So that it is quite common to see rows of cautery marks over the abdomen and spine in these unfortunate patients.

I have seen one case of pellagra in a female patient of about 30 years of age, who, from the gait, the peculiar stoop of the shoulders and tremulousness, looked a clinical picture of paralysis agitans. We have also two male cases at present who on admission were typical pellagrins, having the usual rash and other symptoms. After some months' residence in the asylum the skin peeled off and these patients, to all appearances, became typical general paralytics, with slurring speech, Argyll-Robertson pupil, tremulousness of the tongue and facial muscles, markedly exaggerated knee-jerks, and incontinence of fæces and urine. Both these cases are young men,

not over 30 years of age, and so far as can be observed clinically they have no signs of congenital or acquired syphilis. No symptoms of general paralysis were apparent on admission. (Dr. Warnock has also reported some cases of this description.)[1]

The majority of our cases here are examined post-mortem. The following are the usual microscopic appearances found:

The bodies are always very emaciated, hardly any fat being found. The parotids are always enlarged. The stomach is markedly dilated, denuded of its epithelium, and petechial hemorrhages are nearly always present. All the coats of the stomach are thinned. The small intestine is markedly thinned, presenting an appearance which may be compared to isinglass. It is denuded of its epithelium, and the valvulæ conniventes are less prominent than normal, patechial hemorrhages and a peculiar arborization of the blood vessels are constantly found. The large intestine shows thinning of its coats, with patches of marked congestion and petechial ecchymoses. Signs of Bilharzia are constantly present, especially towards the rectum where bilharzial papillomata are nearly always found.

Intestinal parasites are very common, Ankylostoma, Ascarides, and in some cases tapeworms. Bilharzia worms are nearly always present in large numbers in the portal blood, and sandy patches of Bilharzia are found in the bladder. The lungs as a rule are normal, or show some slight signs of catarrh. The heart is lighter than normal, pale, flabby, anemic and has a peculiar glistening appearance with a marked absence of fat. I have rarely seen atheroma of the aorta or sclerosis of the arteries, in fact it is very uncommon to find atheroma in any of our cases in Egypt even in syphilitics.

The kidneys occasionally are slightly fibrous, but generally are found to be normal, and the capsules nearly always strip easily. The liver and spleen are as a rule normal, but occasionally are slightly fibrous. I have seen two cases of marked bilharzial cirrhosis of the liver in pellagrins. The dura in chronic cases is sometimes found thickened and adherent to the calvarium. In the acute cases it presents a normal appearance. The pia and arachoid generally have a normal appearance; exceptionally they are found milky; they nearly always strip easily, leaving no errosions on the grey matter.

[1]Journal of Mental Science, January, 1902.

The brain is generally of average weight. It is anemic, and in the chronic cases shows some atrophy of the convolutions, especially in the motor and frontal areas. On section the brain is anemic and is softer than normal. The lateral ventricles show some dilatation, and there is generally a slight excess of cerebro-spinal fluid. No granulations have been observed by me, either in the lateral ventricles, or in the floor of the fourth ventricle, nor have I ever observed any marked atrophy of the island of Reil, which has been seen by some observers. The spinal cord shows the usual degeneration of its posterior columns in the cervical region.

Dr. Warnock has observed, and so have I, marked pigmentation of the membranes of the cord, below the medulla anteriorly extending downwards for about an inch. This pigmentation is slightly granular to the touch. I have seen it in a few cases which were not supposed to be pellagrous during life, but it is constant in the pellagrins in this country whom I have examined post-mortem. I have not yet had an opportunity of examining this appearance microscopically, so I cannot give an opinion as to what it is. It may of course be normal in persons with a great deal of pigment, such as our patients have, but as stated above, I have only noticed this pigmentation in pellagrins and in a few others who were not supposed to be pellagrous.

Without wishing at present to enter into the vexed question of the causation of pellagra, I may refer again to the fact that the majority of our cases of pellagrous insanity come from the Delta, where maize is most extensively grown and eaten. In fact, in most places it is the staple diet of the Fellaheen. Fewer cases come from Upper Egypt, where millet is more extensively grown and eaten than maize, and I do not remember having seen a case which came from the Soudan, where millet and not maize is the staple diet. All our cases of pellagrous insanity are Fellaheen; none of our cases come from the big towns where the inhabitants eat very little maize, and being also in a better social position than the poor Fellaheen, can afford a more varied and nourishing diet. I may mention that Dr. Chalmers visited Egypt this spring and informed me that he was unable to find any trace of Simulium in the pellagrous districts which he visited. Our pellagrous patients on being questioned state that their chief food is maize and very often bad maize.

On the other hand we have cases where the rash, intense diarrhœa, and all the other symptoms of pellagra recur in patients who have resided for many years in this asylum, where they have had a diet free from maize. Maize in any form is not allowed in this asylum, and the flour is constantly analyzed to ensure that it is free from maize. Dr. Warnock has also seen such cases in the prisons, where the diet is maize-free, lately millet has been allowed in the prisons but no maize.

Dr. Mott, Director of the Pathological Laboratory of the London County Council Asylums, has suggested that pellagra may be caused in the same way as beri-beri. From a pellagrous district here, I sent two specimens of maize, one good and one bad, and Mr. Mann, of Dr. Mott's laboratory, kindly examined them and reported to me that there was a distinct loss of the lipoid phosphorus in the decayed specimen as compared to the good one. Of course it is too soon yet to attribute much importance to this analysis, as only two samples have been examined, but the research will be continued on these lines. The result of the examination of these two specimens is, however, interesting, as it fits in with Dr. Mott's theory.

With regard to the treatment of pellagra here, Atoxyl has been tried, but the result was not conclusive enough to justify its being extensively used. Our general principles are a maize-free diet and plenty of nourishing meat, vegetables and milk. When the diarrhœa gets severe no drug seems to be of any avail. Fowler's solution of arsenic seems to do the anemia some good. Generally if the case is not too far advanced, the change to more hygienic surroundings and better food does good and a large percentage of our cases are discharged cured; but when they go back to their former surroundings, after a time they recur again and are sent back to the asylum in a worse condition than before. This occurs a few times, and at last they come back to us in a condition of helpless, hopeless dementia.

In conclusion I beg to thank my chief, Dr. Warnock, for his help and kindness in allowing me to use his observations and records extending over a period of seventeen years.

IV. Laboratory Investigations of Pellagra

INVESTIGATIONS OF THE THOMPSON-McFADDEN PELLAGRA COMMISSION.

METABOLISM IN PELLAGRA: A STUDY OF FOURTEEN CASES.

Preliminary Report.

By VICTOR C. MYERS, M. A., Ph. D., and MORRIS S. FINE, Ph. D., Professor of Pathological Chemistry and Instructor in Pathological Chemistry in the New York Postgraduate Medical School and Hospital.

At the instigation of Dr. Wright, Director of the Laboratories at the Postgraduate Medical School, and Capt. Siler and Prof. MacNeal, we undertook early last June the study of the metabolism of the pellagrins who were sent to the Postgraduate Hospital by the Thompson-McFadden Commission.

We have endeavored to make the investigation as extensive as possible; first, because of the desirability of a knowledge of the fundamental processes of metabolism in this disease, and second, because it was hoped that in this way, points of attack would be disclosed which would offer opportunities for more extensive study subsequently. Aside from the work reported by Camurri[1] at the fourth Italian Congress, there appears to have been no attempt at a complete metabolism study.

The general procedures which have been employed in the metabolism study have been to secure duodenal juice and gastric contents (after the Ewald-Boas meal) as soon as practicable after the admission of the patient to the hospital. Subsequently, the patient has been placed upon a carefully weighed and analyzed diet, and the urine and feces collected daily for a period varying from seven to fourteen days.

The duodenal juice has been examined as to reaction, the presence of bile, and lipolytic, amylolytic and proteolytic enzymes.

The examination of the gastric juice has been directed particularly to the determination of the acidities, and the activity of the enzymes, pepsin and rennin.

For experimental reasons, the subjects were in all instances placed upon a practically purine-free, lacto-vegetarian diet, such a dietary being easily controlled and readily lending itself to analysis.

The examination of the urine has included the usual clinical tests, and in addition, quantitative estimations of the total nitrogen, urea, ammonia, uric acid, creatinine, creatine, chlorides, phosphates, inorganic and ethereal sulphates, neutral sulphur, total acidity and indican. Estimations of the sodium, potassium, calcium and magnesium will be completed at a later date in certain instances.

In addition to routine clinical tests, the examination of the feces has been planned to include determinations of water, nitrogen, fat, carbohydrate, ash and the putrefactive products, indole, skatole and phenol.

We have not as yet checked our tests on the duodenal juice with fluid obtained from normal individuals, and are not prepared to make any final statements with regard to the activity of this fluid.

The gastric analyses have shown very interesting results, especially when considered in connection with the indican estimations of the urine. In eight of the fourteen cases, free hydrochloric acid was absent, and in all of these cases, subsequent examinations failed to show the presence of the free acid. The total acidities were low, and pepsin was generally absent, or present only in very small amount. Though considerable amounts of indican were observed in all cases, the quantity was excessive in those with anacidity, reaching in one case nearly one-quarter of a gram per day. Inspection of Chart I[2] will disclose this association of large indican elimination with diminished acidity, and is significant of the increased putrefaction occurring in the intestine when the inhibitory influence of the gastric juice upon bacteria is removed. Johnson,[3] Cecconi,[4] and Niles[5] have recently reported observations on the gastric contents of pellagrins. Johnson found free HCl to be absent in fourteen out of twenty cases; rennin was absent in seven; nausea was present in fifteen, and vomiting in seven; diarrhœa was observed in the fourteen cases with absence of free acid, and present in only one of the other six cases, and here due to another cause. In our own series, the tendency toward the passage of soft stools appears to have been scarcely more marked in the cases associated with anacidity than when free HCl was present, as the figures for the water content of the feces show (Chart I). Cecconi

found free hydrochloric acid absent in all of his twelve cases, while the bile and pancreatic functions appeared to be perfectly normal. The intensity of his qualitative tests for indican seemed to vary considerably, in some cases being intense, and in others, absent. The uniform relationship which we have observed in our own cases between the anacidity and the indican did not appear to exist here, if we are to accept the qualitative tests for indican as representative of the quantitative elimination. From an examination of sixty-four cases of undoubted pellagra, Niles found free hydrochloric acid absent in eighteen, deficient in thirty-one, excessive in twelve and normal in three. He noted that the gastric secretions were diminished or absent in most cases of long standing, while the few where those juices were increased, were acute cases of the disease.

The food intake of all our patients (Chart II)[2], with the exception of Subject 2-M. F., during the first period of observation, and Subject 3-M. McH., during both periods of observation, amounted to between 2,300 and 3,000 calories per day. The intake of Subject 2-M. F. was 1,720 calories and of 3-M. McH., 940 calories during the first period and 1,540 during the second. The nitrogen intake, with the same three exceptions, varied between 12.1 and 18.0 grams, and in all cases a decided plus nitrogen balance was revealed. In Subject 2-M. F., the nitrogen intake was 8.9 grams with a slight plus balance of .6 gram; and in 3-M. McH., first period, a nitrogen intake of 5.0 grams was associated with a minus daily balance of 1.4 grams (Chart III);[2] and in the second period, an intake of 7.2 grams resulted in a plus balance of 1.0 gram. Corn in the form of corn flakes was consumed in all the experiments, while Subject 2-M. F. ate considerable quantities of corn bread during the second period of observation. During this period of seven days she gained four pounds in weight and showed an average daily nitrogen balance of plus 4.1 grams.

The clinical examination of the urine disclosed the presence of a few hyaline casts in six out of the fourteen cases. Of the quantitative determinations, the indican, previously mentioned, was the most interesting, being eliminated in considerable quantities in all cases, but especially in the subjects with inefficient gastric juice. The observations of Cecconi with regard to indican have been mentioned. Tucker[6] reports an increase in indican in three out of fifty-five cases, while in the preliminary report of the Illinois Commission,[7]

the presence of abnormal amounts of indican was noted in some cases. The estimations of the sulphates have not as yet been completed. From the data at hand we have observed in certain instances increased elimination of ethereal sulphates with a high ratio, 1:5, in Subject 3-M. McH., second period. During this period, the indican appeared to be proportionately increased over period one. The volume of urine eliminated and the specific gravity yield values such as one might anticipate with the fluid and food intake, the average volumes varying between 300 and 1,800 c. c., with specific gravities of 1.029-1.013. The figures for total acidity, for chlorides and phosphates are such as we might expect under the given conditions, and the same may be said in general with regard to the various nitrogenous constituents. The values for the total nitrogen, urea, ammonia, uric acid and creatinine were all low, the total nitrogen, urea and ammonia, corresponding with the food intake. This is also true with regard to the uric acid, though here the values are rather low, even for the endogenous uric acid. The creatinine elimination was found to be low in all cases, due probably to the lowered muscular efficiency of the individuals. The urea varied between 8 and 20 grams daily, the ammonia between .3 and .7 gram, the uric acid between .15 and .4 gram, and the creatinine between .54 and .97 gram. When the various nitrogenous constituents were computed in terms of total nitrogen, their percentages were found to vary within normal limits, this being also true of the "rest nitrogen." Eight of the fourteen cases were found to eliminate creatine.

The examination of the feces revealed widely varying conditions as to volume and consistency—watery stools, soft stools, well-formed stools, and hard stools—the average daily elimination amounting to from 60-700 grams of moist feces, yielding 20-40 grams daily of air dry excrement, the moisture varying between 75 and 95 per cent. The daily fecal nitrogen was found as low as .5 gram where the nitrogen intake was low, and as high as 2.7 grams in the reverse condition. In certain instances, the so-called nitrogen utilization was low, *e. g.*, 3-M. McH., 80 per cent. Determinations of the carbohydrates and fat content of the feces have not yet been completed, but the qualitative examination would indicate considerable inefficiency in certain cases. Very strongly positive results were obtained with Schmidt fermentation tubes in certain instances, though the foamy appearance of the feces indicated such a result.

Quantitative estimations of the carbohydrate content will be particularly interesting. The feces of pellagrous patients have a most characteristic aromatic odor, and quantitative estimations of the indole and skatole would indicate that this odor was due to the large amounts of these aromatic bodies. In all instances where the determinations have been made, indole and skatole have been found to be present, though generally the latter was found almost entirely alone or in the largest amounts, averaging in the case of 3-McH., 11 mgms. of skatole daily. The presence of such very large amounts of skatole is unusual and indicative of peculiar bacterial conditions in the intestine.

SUMMARY.

Anacidity is a condition common to pellagra (found in eight of our fourteen cases) and probably accompanies the severe types of the disease. This anacidity is generally associated with an entire absence of pepsin or with pepsin in only very minute quantities. The possibility is not excluded that the gastric inefficiency may be merely incidental or secondary to other factors.

Individuals suffering from pellagra show a marked indicanuria, which is excessive in individuals with gastric inefficiency.

The state of protein metabolism as indicated by the amounts of the various nitrogenous urinary constituents, does not markedly deviate from the normal, though there is slight indication of decreased metabolic activity—low uric acid and creatinine. The elimination of creatine has frequently been observed.

The presence in the feces of phenol, indole and especially skatole in large amounts, together with the high ethereal sulphates and excessive amounts of indican in the urine, point to some unusual bacterial conditions in the intestine.

In certain instances, a slightly defective utilization of both protein and carbohydrate has been observed.

REFERENCES.

[1]Camurri: Atti del Quarto Congresso Pellagrologico Italiano, Udine, 1910, p. 67; see also Preti and Pollini: Zentralblatt fur Biochemie and Biophysik, 1912, xiv, p. 26, which appeared since the present report was made.

[2]These figures will be published in full in the report of the Pellagra Commission; see American Journal of Medical Sciences, 1913, CXLV, p. 705.

[3]Johnson: Southern Medical Journal, 1911, IV, p. 478.

[4]Cecconi: Gazetta Delgi Ospedali e della Cliniche, 1911, XXXII, p. 643.

[5]Niles: Pellagra, New York and London, 1912, p. 77.

[6]Tucker: Journal of the American Medical Association, 1911, LVI, p. 246.

[7]Archives of Internal Medicine, 1912, X, pp. 123, 219.

INVESTIGATIONS OF THE THOMPSON-McFADDEN PELLAGRA COMMISSION.

SOME BLOOD FINDINGS IN PELLAGRA.

By OLIVER S. HILLMAN, M. D., Lecturer in Pathology.

(From the Pathological Laboratory of the New York Post-Graduate Medical School and Hospital.)

The material upon which the following report is based has been obtained from cases of pellagra and specimens of pellagrous blood sent from Spartanburg, S. C., to the New York Post-Graduate Medical School and Hospital, the work being carried on under the auspices of the Thompson-McFadden Pellagra Commission. In spite of the fact that the number of cases investigated is rather small and that the findings are necessarily more or less of limited value, yet it seemed advisable at this time to summarize briefly the more important observations, some of which have been noted by other investigators in this particular field. The blood was examined by standard clinical methods with a view of determining the corpuscle content, the hæmoglobin value, differential leucocyte count, and the structural condition of the blood cells, especially the erythrocytes, in each case. A few observations on the blood-platelet count and on the coagulability of the blood were also made.

ANALYSIS OF FINDINGS.

Two series of cases were examined: In the first, complete blood counts were made, including differential leucocyte counts; in the second series, differential leucocyte counts only were made, owing to the fact that the cases were not under observation in the hospital, the blood smears alone having been obtained and forwarded to the laboratory for examination. Yet in the absence of total leucocyte counts in this series, certain facts were revealed in the differential estimations which tend to a certain extent to substantiate the results obtained in the more complete examinations. The first series comprised twelve cases, in eleven of which two or more examinations were made at intervals varying from one to two weeks.

ERYTHROCYTES AND HAEMOGLOBIN.

Inspection of the tabulated results shows that the erythrocytes on the whole are not markedly altered in number, the average for the series being 4,750,000 per cu. mm.; the lowest count obtained was 3,920,000 per cu. mm., which occurred in a chronic pellagrin, during a second attack of moderate severity. In three cases, counts of more than 5,000,000 red cells per cu. mm. were noted. One of these was an emaciated patient afflicted with pellagra for the first time, and who had a fairly severe type of the disease in which watery stools were a prominent feature. The other two cases were also associated with a high water-content in the stools. It would appear from this observation that the increase in red cells might, in certain instances, be due to a condition of concentration of the blood.

Turning to the hæmoglobin figures, which are in percentage and grams per 100, a greater reduction is seen than is the case in the erythrocytes, the average for the series being 83.8% or 11.7 grams per 100 grams of blood. The lowest reading was 58% (8.1 grams), which occurred in a moderately severe recurrent case of pellagra, uncomplicated so far as could be determined. The highest reading was 107% (14.9 grams), which case had 4,400,000 erythrocytes per cu. mm.; a second reading in this patient showed that the hæmoglobin was well up to par and the red cells only very slightly decreased. The color index was variable, being in the majority of cases, however, below 1. The average was 0.87. Examination of the stained preparation of blood revealed very little change in structure or staining reactions of the red cells; some irregularity in size was noted in a few cases, microcytes appearing to be the most common forms. No nucleated cells were seen.

One is surprised to find in many cases of pellagra, which appear in very poor physical condition and seem anæmic according to our clinical criteria, that the examination of the blood reveals such a small reduction in red cells and hæmoglobin. In spite of some disproportion in the reduction of the erythrocytes and hæmoglobin, noted in a few cases, yet, as a general rule, the changes resemble those of a mild secondary anæmia.

LEUCOCYTES.

The total leucocyte count was within normal limits in six cases; in the other six, a slight to moderate leucocytosis was noted, the highest count being 18,000 per cu. mm., which occurred in a chronic pellagrin running a rather severe course, associated with slight transient elevations of temperature not exceeding 100°; at the time this count was taken, the patient had an extensive pellagrous eruption with areas of superficial infection and was in a very dirty cutaneous condition generally. The count fell to normal coincident with improvement in the skin. The cause of the slight increase in leucocytes in the other five cases was not obvious. Two of these had pellagra for the first time; the other three had recurrent attacks.

The differential leucocyte counts showed the most important and constant alterations (500 cells were counted as routine). In the first series, where total leucocyte estimations were made, a lymphocytosis was revealed in eight cases at some time during the period of observation; in most of these cases the lymphocytosis was a constant feature. For purposes of classification the leucocytes were divided into polynuclears, small lymphocytes, large lymphocytes, large mononuclear leucocytes of Ehrlich, transitional forms, eosinophiles and basophiles. The cells increased were chiefly the small lymphocytes. Including both large and small types of lymphocytes the percentages in the more pronounced cases ran as follows:

43.00%
36.00%
50.35%
47.20%
52.00%
41.80%
40.00%

Some of these cases had a leucocytosis which would mean that the lymphocytes were absolutely increased. More data on this point will be necessary before coming to any definite conclusions. It may be said, however, that the majority of pellagrins show a relative increase in the lymphocytes at the expense of the polynuclear neutrophiles. As to the large mononuclear leucocytes, the differential counts show, on the whole, a slight increase in most cases, rising as high as 5.6% in one instance. No definite correlation could be

determined in such cases between this mononuclear increase and the clinical symptoms, or stage of the disease. The polynuclear eosinophiles maintained a normal average in most cases, but in three were in excess, amounting to 8.00%, 7.80% and 5.40%. Other causes of eosinophilia were not demonstrated in these patients. The average eosinophile count in this series was 2.86%.

In the second series of fourteen cases where differential leucocyte counts were not available, lymphocytosis at the expense of the polynuclears was found in thirteen cases; the remaining case showed practically a normal count. The large mononuclear leucocytes were slightly increased, the average being 1.97%; the eosinophiles averaged 2.82%. Two patients in this series exhibited an eosinophilia, one of 9.00% and the other of 7.00%. The stained blood slides were carefully looked over for the presence of abnormal cells and organisms with negative results. Blood-platelet counts were made in two cases and found to be within normal limits. The coagulation time was determined in one case in which the blood showed considerable viscosity, and was found to be unaltered. Three other observations on this point gave the same results.

DISCUSSION.

The blood in the majority of cases of pellagra shows a moderate anæmia of the secondary type. Whether this is due to the actual attack of the disease or is the result of a train of antecedent conditions extending over some period of time, is difficult to say from such a small series of cases. The increase in lymphocytes is interesting and what one might expect in a disease associated with a disturbance in gastro-intestinal function and structure. It is a well known fact that lymphocytosis is not uncommon in poorly nourished, cachectic individuals. In pellagra we probably have to deal with a disease associated with a rather low grade toxin of some nature, which, in common with many other pathological states, is absorbed by the lymphatic system and through local irritation of certain lymph nodes produces an increased circulatory activity in these situations, in consequence of which large numbers of lymph elements are swept from the lymphatics and enter the general circulation. This is in accordance with Ehrlich's theory of lymphocytosis. The large mononuclear leucocytes are not sufficiently increased to warrant drawing any definite conclusions. More information is

desirable on the condition of the leucocytes in pellagra, especially the differential estimations. Work along this line will be continued at the New York Post-Graduate Medical School and Hospital and we hope to be able to report at some future date a larger and more conclusive series.

INVESTIGATIONS OF THE THOMPSON-McFADDEN PELLAGRA COMMISSION.

Further Observations Upon a Bacillus Isolated from the Feces of Pellagrins.

By W. J. MacNeal and Nannie B. Hamilton.

(From the Laboratories of the New York Post-Graduate Medical School and Hospital.)

During the course of a somewhat systematic study of the intestinal bacteria of pellagrins undertaken by the Illinois State Pellagra Commission in 1910 and 1911, a number of bacterial strains were isolated. Approximately one hundred of these bacterial strains were subjected to agglutination tests with the blood serum of pellagrins. Two of the cultures, namely those designated as No. 14 and No. 67, behaved in a somewhat interesting manner in these tests, showing very definite positive agglutination with the sera of acute cases of pellagra, and more uncertain results with the sera of pellagrins during the interval between the attacks. The suggestion of a possible relationship between these bacteria and the disease was very much weakened by the occurrence of agglutination with the sera of insane patients free from pellagra, and with the sera of normal individuals, in many instances as definite as that obtained with the sera of pellagrins. The meaning of the results was, therefore, obscure, but, nevertheless, these bacteria seemed worthy of further study. In their biological properties the two strains, No. 14 and No. 67, seemed to be very closely related if not actually identical. A summary of these results has appeared in the August number of the Archives of Internal Medicine.[1]

In our study of pellagra at the New York Post-Graduate Medical School, it seemed desirable to devote some further attention to these bacteria. This was more especially indicated because the previous agglutination tests had all been performed with sera of individuals in Illinois, and the suggestion of a relationship to pellagra may have been due merely to some locally prevalent infection

[1]Pellagra in Illinois. Arch. Int. Med., August and September, 1912, X, 123 to 168, 219 to 249; Report of the Pellagra Commission of the State of Illinois, Springfield, Illinois, 1912.

with this organism. The opportunity was now presented to test these bacteria with the sera of pellagrins in an entirely different locality far from the region where they had been isolated. Obviously, the occurrence of negative results in these new tests would stamp the organism at once as a local incident, while if positive results should again be obtained they would tend to strengthen the suggestion that this organism might bear some relation to pellagra, either as a primary factor in causation or as an important secondary invader.

As a preliminary step in this work, an attempt was made to obtain further evidence concerning the possible identity of the two strains, No. 14 and No. 67. Each organism was cultured in broth, and then repeated large doses of the broth culture of each was injected into a rabbit. The rabbits weighed 1,837 and 1,660 grams, respectively, the first receiving 20 cc. of the broth culture of Strain No. 14 subcutaneously on two occasions, May 21 and July 8, and the second being injected at the same times with similar doses of Strain No. 67. The animals lost some weight as the result of this treatment, but apparently were not made very ill. After this treatment it was found that the blood serum of either rabbit served to fix complement equally well in the presence of an antigen prepared from the cultures of either strain, indifferently. This evidence, together with the agreement in behavior of the two in cultures on agar, in milk, in gelatin, and in fermentation-tube cultures in broth containing the various sugars, seemed sufficient to warrant us in regarding them as different strains of the same bacterium, at least for the present.

The strain No. 67 has been regularly employed in the agglutination tests at New York this past summer. The work is still in active progress, and we are not in a position to render any final report upon it at this time. We wish, however, to present the results obtained with the serum of 106 pellagrins of South Carolina, chiefly resident in Spartanburg county, and results obtained with serum of 43 control individuals, 16 of whom were residents of South Carolina and the remaining 27 residents of New York. The cases of pellagra have been divided into two groups, those showing the eruption at the time the blood was drawn and those without the eruption present.

There are 63 cases in the series showing the eruption when the blood was taken. Of these, 48 gave complete agglutination and precipitation of the agglutinated bacteria to the bottom of the tube in a dilution of one in ten at the end of one hour. This grade of reaction has been designated as complete. Five of the 63 sera gave a reaction almost as marked as this, but the supernatant liquid was not entirely cleared. This grade of reaction has been designated as almost complete. Three of the 63 gave reactions designated as marked. In these the bacteria were clumped into flocculent masses at the end of the hour, but had not yet been precipitated to the bottom. Three of the 63 sera produced a reaction designated as slight, and four gave negative reactions. These require no special description. The results for these sixty-three sera from cases of pellagra showing the eruption, were, therefore, as follows:

Total Cases.	Complete.	Almost Complete.	Marked.	Slight.	Negative.
63	48	5	3	3	4

The four cases which gave negative reactions were reported as showing desquamation only, and of the three which gave the slight reactions, one was reported as showing acute erythema and the other two as showing desquamation. Further details concerning all these cases we hope to incorporate in a later report.

In the series of pellagrins without eruption at the time the blood was taken, there are 43 cases. The results for these sera were distributed as follows:

Total Cases.	Complete.	Almost Complete.	Marked.	Slight.	Negative.
43	30	6	0	0	7

Of the seven negative cases, four gave a history of eruption during 1912, from two to five months before the blood was taken. The other three were not known to have had a recurrence of the eruption since 1911.

The total figures on the 106 cases of pellagra, including those with eruption and those without eruption at the time the blood was taken, were, therefore, as follows:

Total Cases.	Complete.	Almost Complete.	Marked.	Slight.	Negative.
106	78	11	3	3	11
	74%	10%	3%	3%	10%

In the series of control sera from Spartanburg county, South Carolina, there were 21 cases. The results for these were distributed as follows:

Total Cases.	Complete.	Almost Complete.	Marked.	Slight.	Negative.
21	6	0	3	6	6

Some doubtful cases have been included in this table, individuals showing roughness of the hands and forearms, or giving a history of a suspicious sunburn earlier in the year. Three of the sera giving complete agglutination were from cases of this kind. Most of these sera were sent to us for the Wassermann reaction, and they have been used as controls for this work in agglutination.

There were 27 individuals in the series of controls from New York. The results of the agglutination tests on these sera were distributed as follows:

Total Cases.	Complete.	Almost Complete.	Marked.	Slight.	Negative.
27	6	3	10	1	7

Most of these were dispensary cases sent to us for the Wassermann test. Three of the sera were obtained from members of the laboratory staff, and of these two gave reactions designated as marked and one gave a negative result.

Bearing in mind the fact that agglutination tests are sometimes indefinite and inconsistent in certain diseases in which consistent positive results may be obtained by resort to other serum reactions, we have made a beginning by trying to perfect a complement-fixation test, using an antigen prepared from cultures of the bacterial strain No. 67. The work along this line is still too incomplete to be reported.

A limited number of cutaneous tests and intracutaneous tests have been made. For the cutaneous tests an old broth culture of Strain No. 67, killed by heating to 60° C. for an hour and preserved by the addition of 0.5% carbolic acid, was employed. A drop of this was applied to a shallow incision on the skin and rubbed in with a glass rod. Two other similar incisions were made at the same time as controls, and tuberculin was applied to one of these while the other was left without any application. The results of these tests were as follows:

Patient.	Strain No. 67.	Control Blank.	Tuberculin.
E. C.	Moderate	Negative	Slight
M. L.	Slight	Negative	Marked
M. T.	Negative	Negative	Negative
L. G.	Slight (?)	Negative	Moderate
M. S.	Negative	Negative	Slight
B. B.	Negative	Negative	Very marked
M. L.	Slight	Negative	Slight
C. M.	Negative	Negative	Negative
B. B.	Negative	Negative	Negative
A. N.	Negative	Negative	Negative

Of the nine cases, four gave evidence of reaction to the culture and six reacted to the tuberculin. The one case, B. B., showed tubercle bacilli in the sputum and there was physical evidence of moderately advanced lesions in the lung.

The first intracutaneous tests were made by injecting a rather heavy suspension of the killed bacilli in a dose of 0.1 cc. into the substance of the skin. Three pellagrins and two normal individuals were tested, with the following results:

Patient	24 hours	48 hours	72 hours	Result
S. (N.)	Slight	Subsiding	Faded	Negative
M. (N.)	Slight	Slight	Subsiding	Negative
M. T.	Slight	Slight	Faded	Negative
E. C.	Slight	Moderate	Moderate	Moderate
M. L.	Slight	Slight	Moderate	Slight

The first two were normal individuals, members of the laboratory staff.

For the subsequent intracutaneous tests, a standardized vaccine containing one thousand million killed bacilli per cubic centimeter was employed. A dose of 0.25 cc. was injected into the skin. The amount of fluid in this dose was larger than in that used for the preceding injections and therefore more accurately measurable. The amount of bacterial substance was very much less, probably less than one-tenth the amount contained in the former dose. One normal individual and seven pellagrins have been tested with this dose, one of the latter on two occasions. The results obtained were as follows:

Patient	24 hours	48 hours	72 hours	Result
M. (N.)	Slight	Slight	Faded	Negative
L. G.	Slight	Slight	Slight	Slight
M. S.	Slight	Slight	Fading	Negative
B. B.	Moderate	Slight	Slight	Slight
M. L.	Moderate	Slight	Slight	Slight
E. C.	Marked	Marked	Marked	Marked
C. M.	Negative	Negative	Slight	Negative
B. B.	Slight	Slight	Faded	Negative
A. N.	Marked	Marked	Subsiding	Marked

The variation in the results of these tests seems to bear some relation to the severity and the stage of the pelagrous eruption, but the series of observations is, of course, too limited to warrant conclusions. The two cases showing the marked reactions were well-nourished individuals just recovering from rather severe attacks of pellagra of short duration. The case showing the least reaction, C. M., was a very severe chronic case, exhibiting profound exhaustion with delirium, after the erythema had ceased to extend and had desquamated for the most part. The case B. B., which was tested twice, was a mild chronic case. The slight reaction was obtained while the eruption was present on the wrists, and the second test, which gave a negative result, was made after the eruption had disappeared and just before her discharge from the hospital. The results of the cutaneous and intracutaneous tests also show a relative agreement except in the one case A. N. In this case the two tests were made at the same time on the same arm, and the marked reaction to the intracutaneous test may have obscured any possible reaction to the cutaneous test, as the latter was included in the reddened and swollen area.

At the same time that these experiments with this culture were in progress, we have undertaken to isolate further strains of bacteria from the intestinal contents of pellagrins. These have been obtained by making plate cultures on plain agar, ascitic-fluid agar, and blood agar, inoculated with feces of pellagrins and with intestinal juice obtained from our cases through the Einhorn duodenal tube. Colonies were fished from these plates and subsequently tested by culture in gelatin, in litmus milk, and in fermentation tubes of glucose broth, and finally by subjecting each strain to agglutination tests with the sera of pellagrins. In this way 693 strains of bacteria have been isolated during the summer, and these

have been tested by approximately 2,000 agglutination tests. This part of the work is still far from finished. So far there have been found among these 693 cultures, 70 strains which have given suggestive agglutination reactions at one or more tests. These have been set aside for more detailed study. Six strains have been found which agree in the preliminary culture tests with the Strain No. 67, but which have so far failed to give positive agglutination tests.

The observations reported in this paper seem to us too discordant and too incomplete to warrant any definite conclusions. We expect to pursue the work along the lines indicated here, and hope eventually to be able to express an opinion concerning their interpretation. At present the results are not very definitely positive, yet, inasmuch as they are not very definitely negative either, it would seem unwise to neglect this field of study.

STUDIES OF THE METABOLISM OF MOULDS BELONGING TO THE GENUS PENICILLIUM.*

By C. L. ALSBERG and C. F. BLACK.

(Bureau of Plant Industry, U. S. Department of Agriculture.)

Mr. President, Members of the Association:

The Poisonous Plant Laboratory of the Bureau of Plant Industry, U. S. Department of Agriculture, has been directed by the Secretary of Agriculture to undertake the investigation of the causes of various intoxications of man and animals attributed to the products found in maize after moulds have developed on the constituents of the corn kernel. This must be a matter of great concern to the Department of Agriculture since it threatens to affect as an article of diet the value of maize, the country's chief crop.

The situation has demanded four series of investigations. The first deals with the conditions of growing, harvesting, curing, storage and transportation, leading to the deterioration of maize and with the methods of preventing deterioration. This study is pursued for the most part in the Division of Grain Standardization of the Bureau of Plant Industry.[1] The second deals with the methods of detecting the deterioration of maize. Some of the results have already been published,[1] and the methods outlined are in use by State officials in charge of corn inspection, notably by the Hon. E. J. Watson, Commissioner of Agriculture, Commerce and Industries of the State of South Carolina.[2] The third series of investigations deals in greater detail with the chemical composition of maize. Such information is needed in order that the genesis of the products formed in the process of spoiling by moulds may be understood. The results of these researches are not yet published. The fourth series of these investigations deals with the composition and alleged toxic action of spoiled maize. It is a part of this fourth series of investigations that I wish to present to you today.[3]

To investigate by time honored procedures the alleged toxic action of maize spoiled by moulds seemed to us a valueless task, since none of the labors of our predecessors have yielded universally convincing results. There are a number of reasons for the discordant

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results obtained by them. The earlier investigators used accidental mixtures of moulds grown on complex and variable media, such as unsterilized maize, wheat or bread, so that their results can no longer be reproduced. Though later investigators employed cultures upon synthetic media, in most instances their results can not be duplicated because it is not possible to identify the moulds employed. Thus most of those studying *Penicillium* were content to describe the organism as *P. glaucum* Link. Under this name the mycologist Link described so vaguely a green-spored species of *Penicillium* that no man can say today what organism Link would thus identify. For this reason the mycologist, Dr. Chas. H. Thom, of the Storrs Agricultural Experiment Station, in monographing the genus *Penicillium* was compelled to discard the name "*P. glaucum*."[4] In fact he recognizes a considerable number of species with green spores. Which species were used by the different investigators studying the toxicity of *Penicillium* it is not possible to say. To avoid any confusion from such a cause in the investigations of Gosio, Dr. C. H. Lavinder, of the Public Health Service, at our request, very kindly endeavored to procure cultures from Prof. B. Gosio, of Rome. Professor Gosio very courteously replied, writing that, unfortunately, circumstances had prevented him from keeping the cultures alive.

It was consequently concluded that the most profitable study would be the products resulting from the growth of identified moulds upon definite synthetic media under known conditions, rather than the duplication of the work of former investigators who used unidentified organisms often grown on variable media, such as maize meal. From among the many types of moulds which have been found on spoiled maize those of the genus *Penicillium* were selected for study for the very practical reason that this genus, owing to the studies of Thom, is now well known; and, further, that Dr. Thom generously offered both to furnish and to identify cultures for us. The cultures themselves were kindly made by Dr. Erwin F. Smith.

A preliminary study of nine species of *Penicillium* obtained from spoiled maize was made in order to select one or more species for intensive study. The moulds were grown upon sterile corn meal, and by methods described elsewhere[5] were examined both for toxicity and for the occurrence of the phenolic substances alleged by

Gosio to be present. Gosio's publications do not contain sufficient evidence to warrant his assumption that among the metabolic products of moulds phenols occurred, for he did not study them sufficiently chemically. He based his opinion very largely upon the fact that extracts of moulds or mouldy material gave a red, violet, purple or green color with dilute solutions of ferric chloride. It is the reaction most of you have used for the detection of that pharmacopœial phenol, salicylic acid.

Two of the nine moulds examined produced, when grown on sterile corn meal, products toxic to white mice. One of these gave no phenol reaction; the other, *Penicillium puberulum* Bainier, gave the reaction with a red color. A third species, *Penicillium stoloniferum* Thom, though not toxic, gave this reaction with a violet color. It was decided to study intensively the two species named because it is believed by Gosio and others that the toxic substances produced by moulds are phenols and that pellagra is a chronic intoxication by these phenols.

These substances giving the color reactions were isolated. From cultures of *Penicillium puberulum* upon Raulin's medium a new acid of the empirical formula $C_8H_{10}O_4$ giving a red color with ferric chloride, was isolated. Provisionally the name penicillic acid is suggested for it. From similar cultures of *P. stoloniferum* a second new acid of the empirical formula $C_{17}H_{20}O_6$, giving a violet color with ferric chloride in aqueous solution, was isolated. The name mycophenolic acid is suggested for it. It is not necessary here to repeat to you a description of the methods by which these acids may be prepared nor to give a description of the chemical studies to which they were subjected. These will be published elsewhere.[6] It will suffice to say that the chemical examination leads us to suspect that these acids belong to the class of substances named lichen acids, because they were believed to be found only in lichens. The occurrence of similar substances in fungi, while interesting, is not astonishing since lichens are symbiotic growths composed of fungi and algæ.

In one important respect these two acids differ from each other. Only penicillic acid is toxic. Seven milligrams injected subcutaneously suffice to kill a white mouse of twenty-five grams weight. The first symptoms noted are convulsions which gradually disappear, the mouse dying after some hours from progressive weakness.

The lethal dose for guinea pigs is somewhat less proportionately, being two-tenths to twenty-five hundredths of a gram per kilo. In guinea pigs the only symptoms are progressive weakness. The toxic dose of penicillic acid lies, therefore, between that of salicylic acid and that of carbolic acid.

The amount of penicillic acid produced by the organism in three to four weeks' growth is about twenty-five hundredths of a gram per culture of about 700 cc. of medium. The amount produced is therefore so small that it can hardly cause acute intoxications except in laboratory experiments. Nevertheless, penicillic acid is apparently more toxic than is the "pellagrozein" of Lombroso. Moreover the properties of penicillic acid are such that if it was formed by the moulds growing in the maize examined by Lombroso this acid must have been present in his "pellagrozein." While penicillic acid is not likely under ordinary conditions to produce acute intoxications, it is not possible to say that it may not produce chronic intoxications, or that its action is not cumulative. Unfortunately, the difficulties of obtaining large amounts of the acid are as yet so great that these questions have not been completely investigated. At present the data are, therefore, lacking for any decision of the question whether it is or is not a factor in the causation of pellagra.

While mycophenolic acid is not toxic, for another reason its occurrence is of interest. The organism which produces it was obtained from a sample of condemned maize very kindly procured for us in Italy by Dr. C. H. Lavinder. It was identified by Dr. Thom as *Penicillium stoloniferum* and is the only organism from Italy hitherto examined by us. For purposes of comparison we secured from Dr. Thom a specimen of his type culture of *P. stoloniferum*. While cultures of this organism were apparently nearly identical morphologically with the organism obtained from the Italian corn, it did not produce any detectable quantity of mycophenolic acid. It did, however, produce a substance or mixture of substances giving the phenol reaction with the same tint as mycophenolic acid. As this material has not yet been obtained in satisfactory crystalline form not much can be said about it at present.

Since the type culture of Dr. Thom was an old one, having been propagated in the laboratory for several years, it seemed possible that its power to form mycophenolic acid might have been weakened by long artificial propagation. In order to test this hypothesis we

examined a third strain kindly isolated for us by Dr. Thom from soil in the spring of 1912. It was found to produce neither mycophenolic acid nor any substance giving the phenol reaction with ferric chloride. Therefore, there is no evidence that through age the type culture failed to produce mycophenolic acid.

We have, therefore, three strains of apparently the same organism yet different in respect to the production of mycophenolic acid. One produces this acid; from cultures of a second we have not yet succeeded in isolating it, though other substances giving a violet color with ferric chloride are formed. A third has as yet produced neither mycophenolic acid nor any substance reacting with ferric chloride. Whether these three organisms are to be regarded as identical or as different strains or "physiological varieties" still remains unsettled. Apparently in dealing with moulds we are confronted with the very difficulties with which the bacteriologist has to contend. The species and varieties of moulds are far more numerous than supposed and far more difficult to distinguish. These facts alone account for the discrepancy in the reports of most investigators, and they warn us to suspend judgment on the alleged toxicity of moulds until a great number of them have been investigated under a great variety of conditions.

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BACTERIOLOGICAL INVESTIGATIONS IN PELLAGRA.

By DR. EUGENIO BRAVETTA, First Assistant Physician, Provincial Asylum of Milan, Mombello, Italy.

The bacteriological study of the blood and of the cerebro-spinal fluid in pellagra has received a notable impulse from the researches of Prof. Tizzoni, who has published a new doctrine on the much discussed question of the etiology of this disease.

Repeatedly, in the past, various investigators have tried to isolate a possible specific micro-organism of pellagra. Majocchi, in 1881, a *schizomycete,* which he called *bacterium maidis,* and which is one of the germs isolated from spoiled corn. Cuboni also found it later in the feces of pellagrins.

These results have been contradicted by Paltauf and Heider, who isolated from spoiled corn innumerable varieties of germs; and by A. Monti, who, in a systematic study of micro-organisms which may be found in spoiled corn, has drawn the conclusion that, for the production of maidic poisons, not only bacilli must be taken into consideration, but also saccharomycetes and moulds to whose complex action must be attributed the various putrefactive and fermentative processes which affect corn and the consequent production of a poison, of a chemical or biologic nature which has a special affinity for the nervous system.

Carraroli isolated from spoiled meal a bacillus which he claimed was the specific agent of pellagra, and called by the name of *bacillus pellagrae.* Fossati cultivated from corn bread, even after baking, a *streptococcus* and a *bacillus* similar to *b. coli,* the former capable of producing in animals severe forms of enteritis, the latter liable to increase the pathogenic property of *aspergillus fumigatus.* P. Marie has observed in pellagrins, with a certain constancy, a micrococcus, which, however, he has not been able to cultivate. Sambon has not yet found in pellagrins either protozoa or metazoa which had any relation to the disease in question. Low repeated the same experiments and extended them to the spirochætæ and to the filariæ, but always with negative results. Lavinder, using the technique advised by Tizzoni for bacteriological examination of the blood and propagating cultures by the most varied means, has always had

absolutely negative results. The Illinois commission also made blood cultures, but with negative results in all the cases.

At the end of the year 1906, Tizzoni and Fasoli stated that they had succeeded in isolating from the blood, from the cerebro-spinal fluid and from the organs of persons affected with, or dead from, severe pellagra, a micro-organism which they affirmed to be the sole cause of pellagra. In numerous successive published articles Tizzoni has confirmed and extended his researches, setting forth in detail the morphological, cultural and biological characteristics of this specific germ which he calls *streptobacillus pellagrae.*

Also from the blood of infected guinea pigs, from the feces of pellagrins and from spoiled corn, Tizzoni has succeeded in isolating the specific germ, which he thinks is very pathogenic for the common laboratory animals, and also for monkeys in which, as in guinea pigs, it is able to reproduce the clinical picture and pathological anatomy of pellagra.

In the last few years, Tizzoni has studied, in collateral investigations, the power of resistance to high temeprature, of the *streptobacillus pellagrae;* he has demonstrated the existence of a specific precipitine in the blood of pellagrins, and initiated the first experiments in vaccination of animals against the specific germ. Furthermore, a few months ago, Tizzoni asserted that in the blood of pellagrins there exists an *anti-hemolysine* which antagonizes the hemolytic power of the normal heterolysines, and this he claimed established the existence of an immunizing reaction of the blood which indicates the infectious nature of the disease, and likewise establishes a connection between such reaction and the hemolytic power of the specific germ isolated by him.

But I am compelled to state that the experiments conducted at Mombello by Professor Tizzoni himself under better conditions for experimentation for the purpose of proving the existence of this very immunity reaction in pellagrins, have completely failed.

At any rate all these recorded researches which Tizzoni, for many years, has continued persistently to set forth in strict scientific garb, have not been able to arrest the attention of pellagrologists even though, by merit of these researches, Tizzoni was honored with membership upon the Italian Ministerial Commission for the study of pellagra.

But on the one hand the existence of the *streptobacillus pellagrae* has been confirmed by Ramella and by J. Wolfe and by Wood, while

on the other it is, in turn, emphatically denied by A. Perroncito, by Cesabianchi and by Terni and Fiorani (1911).

Last spring, the Italian Ministerial Commission was divided into different subcommissions which were charged with the duty of making up a suitable program of investigations, and the subcommission for Lombardy composed of Bertarelli, Antonini and Tizzoni, proposed for itself, among other things, the control and extension of the observations of Tizzoni, extending them especially to cases of ordinary pellagra and to hereditary pellagra.

The subcommission of Lombardy at the session of June 8, 1912, reported unanimously to the Commission assembled at Rome concerning the recent bacteriological studies relative to the germ already previously isolated by Tizzoni, and concluded by affirming that they had succeeded in isolating from the blood of some pellagrins, and, in one case also, from the cerebro-spinal fluid, forms of streptococcus and of streptobacillus identical with those described by Tizzoni, with cultural characteristics strictly hemophilic and of rather slow development. However, they refrain from giving a definite judgment, declaring that they are not able, at present, even to determine the importance of such results, either from the strictly scientific or practical standpoint, *e. g.*, a diagnostic criterion, if they should be confirmed by later experiments.

A very recent and noteworthy contribution to the pathological anatomy and experimental pathology of pellagra from the hand of Dr. G. Veroni, assistant of Tizzoni, fixes the preponderating importance of the *streptobacillus pellagrae* in the pathogenesis of pellagra by demonstrating that as the symptomatology of the disease, which is reproduced experimentally in animals by the inoculation of the *streptobacillus pellagrae* resembles in very many of its characteristics the pellagra of man, so the anatomical changes of this experimental form, through their nature, course and localization, show, in the majority of cases, an incontrovertible analogy with the corresponding human changes.

I have had the opportunity of following, close at hand, a great part of the investigations of the Ministerial subcommission, and, by courtesy of Prof. Tizzoni, to learn the technique followed by him in order to isolate and cultivate the *streptobacillus pellagrae,* and I afterwards continued, for myself, these interesting experiments.

The constancy of the results obtained makes it possible to give a résumé of my experiments in a few words.

I have, in the asylum at Mombello, examined the blood of 42 pellagrins in all of the different stages of the disease, from the initial or light forms to those old or relapsing, or even severe cases which carried the patients rapidly to death; and in all these cases the search in the blood, and in 10 cases also in the cerebro-spinal fluid for the *streptobacillus pellagrae,* resulted negatively. In several cases of hereditary pellagra the examination was also negative.

It is indeed true that in a very small per cent. of the patients I was able to isolate cocci united in a mass, or again into short or long chains, very similar to the two types of the specific germ described by Tizzoni, and staining (as the latter has recently stated also for his *Streptobacillus pellagrae*) by Gram's method; but the morphological and cultural characteristics show that one has here before him always the common pyogenic micro-organisms with which the cultures had been contaminated. Also inoculations in common laboratory animals never produced the clinical picture of pellagra. As a control, I then determined to examine, with the same technique, the blood of 18 persons, either sound or presenting lesions of the skin or of the intestines or nervous system, similar to those of pellagra (alcoholic, solar or senile erythemata; forms of diarrhœa, of progressive paralysis, etc.), but certainly not pellagrous, and even some living in the asylum ten or more years. Also in these cases the bacteriology of the blood showed a negative result, except in one in which I isolated a micro-organism which proved to be a staphylococcus pyogenes.

Here I ought to mention that some of these specimens of blood coming from nonpellagrous persons, were sent by me to Bologna to Prof. Tizzoni; and that in one of these Tizzoni succeeded in isolating his typical *Streptobacillus pellagrae,* of which a little afterward he sent me two specimens of the culture; so that in an indirect way he claims to have demonstrated that the *Streptobacillus pellagrae* is not found exclusively in pellagra, and therefore one cannot speak of specificity.

From what I have thus set forth the following conclusions may be drawn:

I. A *Streptobacillus pellagrae* does not exist.

II. The blood and cerebro-spinal fluid of pellagrins are sterile.

THE NERVOUS HISTOPATHOLOGY OF PELLAGRA.

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The records of the study of the nervous histopathology of pellagra by modern methods of staining are still somewhat meagre and this was considered to be sufficient justification for the publication of this paper. The findings have been purposely somewhat summarized for presentation at this meeting and the details will be published subsequently in a more extensive article.

The material comprises altogether 15 cases, although in one, the only points studied were the nerve cells. They include the cases which form the basis of the incomplete study published in the Report of the Illinois Pellagra Commission. In some respects this material is not very satisfactory in that all but two of the cases were suffering from some mental disorder, five were examples of senile dementia, two of chronic alcoholism. There were three cases in which the pellagrous symptoms had ceased some months before death, which took place as the result of intercurrent disease. All three of these cases, however, were also suffering from chronic mental disorder and it would have been of great value if we had been able to include the study of one or more interval cases uncomplicated by such brain disturbance. We would here state that we should be extremely grateful to any physician who can furnish us with the nervous system of such cases. The number of cases here in the South is unquestionably much greater than that in Illinois and opportunities for obtaining such material must certainly occur.

The methods of staining employed were: Hæmatoxylin and eosin, van Gieson, thionin and toluidin blue, Unna-Pappenheim, Herxheimer-Daddi, nilblue sulphate, osmic acid and toluidin blue, Weigert's elastic tissue stain, Mallory's glia stain, Alzheimers' Methods IV and V, Bielschowsky silver impregnation, Wolters-Kultschitzky and Marchi myelin sheath stains.

With regard to the gross pathology there is but little to be said, the changes found being the accompaniment of the concomitant disease rather than due to pellagra. Arachnitis ossificans in the spinal membranes has been recorded by several authors and was present

in two of our cases, but this is also met with in other diseases, such as general paralysis, and seems of little importance here. We might especially emphasize, however, the absence of punctate hemorhages and focal softenings in all cases.

The *Pia Mater* was studied in 13 cases. The changes were sometimes so slight as not to be notable. In most there was more or less thickening, with increase of fibro-blasts and infiltration with cells chiefly derived from the vessels, both endothelial and adventitial. In some there were a few lymphocytes and occasionally extravasated red cells. Pigment granules of fatty and fibrinoid character were constant. In most cases the change was most marked over the convexity of the brain in the central, frontal and temporal regions, and also especially in and around the sulci. In a few there was a growth of glial fibres into the pia, especially in the sulci. In only one case were these changes severe and in this it was universal, involving even the cerebellum.

The chief deviations from the normal in the pia concerned more especially the vessels. In the larger arteries, in a few but not all of the cases, there was thickening of the walls with hypertrophy of the muscularis. In two cases there was also curling and twisting of the intima. The smaller vessels in all cases showed more or less proliferation of the cells, endothelial, muscular and adventitial, and there was generally a small amount of perivascular infiltration consisting of vessel cells and lymphocytes. Plasma cells were absent in all but two cases and in only one of these were they at all frequent. In this case, referred to again in discussing the vessels of the brain, the pial changes of all kinds were marked but not, in any degree, to be compared with those found in general paralysis of the insane. No basophil cells were found in any case. There were no new formed vessels. No hyaline degeneration was found in any of the cases and in only one did there seem to be a possible thrombosis.

In all cases pigment granules of fatty and fibrinoid nature were present in the vessel sheaths together with a greater or less number of fat-laden Abraümzellen.

Vessels. The vascular changes may be subdivided into two groups, chronic and acute. The former were present only in those cases of 50 years of age or more, with one exception, a man of 41 with a history of chronic alcoholism. They consisted of thickening

of all coats of the larger arteries with splitting of the intima. In only two of these was any hyaline change found, one being a case of senile dementia aged 67 and the other of chronic alcoholism. In none of the cases were any occluded vessels observed and in only one, a man of 67 with severe senile dementia, was there found any evidence of focal vascular lesion. This brain showed scattered patches of subcortical degeneration, probably of vascular origin. In none were found anything suggesting an *état criblé*.

At this point it would be well to describe the vascular changes found in the three interval cases. All showed chronic changes in the walls of the large vessels similar to those described above. In two of these muscle and endothelial cells were found lying within the spaces formed by the splitting of the intima. Both of them had died with acute infections, lobar pneumonia and acute tuberculosis. In the small vessels two cases showed thickening and proliferation of the coats. In one there was very little exudate, while this was more marked in the other two. One of these showed evidence of the acute infective process (acute tuberculosis), by the presence of leucocytes and blood cells. In this case also there were numerous plasma cells, equal in number to the lymphocytes. It is interesting to note that the only other case of the whole series in which plasma cells were found was also an interval case dying from tuberculosis, although here the disease was more chronic and there were no blood cells in the perivascular exudate. The exudate in these three cases consisted of lymphocytes, vessel cells, Abraümzellen and pigment granules.

The changes described above have probably little to do with the pellagrous disorder.

The more acute changes found in the smaller vessels of those cases (11) dying during, or soon after, acute outbreaks of pellagra, may probably be considered as having a closer relation to that disease, although the conditions of age and alcoholism must not be forgotten. These changes consisted of a moderate proliferation of the cells of the adventitia and media, present in all, with less marked increase of intima in a few. The muscle cells in many instances were swollen, distorted, poor in chromatin and contained pigment granules. Where the intima was involved the cells were shrunken, darkly staining and also contained pigment. The perivascular spaces were widened in three senile cases and in one of chronic

alcoholism. In all cases there were present in the sheath fatty and fibrinoid pigment with Abraümzellen, or granule cells, containing fatty and to a less degree fibrinoid particles. In one case there was no other perivascular infiltration and in two more the infiltration was extremely slight. All others showed more or less infiltration. Vessel cells were found in all, lymphocytes in 6 of the 10 (in two of these only in very small numbers). No plasma, mast, nor blood cells were found in any of these cases.

Stäbchenzellen were rare in all cases and in none exceeded the normal limits.

New vessel formation was observed in three of the recent pellagra cases but only in small numbers, a close search being necessary to find them at all in two of these. A few new vessels were also noted in one of the interval cases dying from chronic tuberculosis. Twisting of the vessels were present in three cases of chronic alcoholism and senility, while rope-formation due to the intertwining of three or four vessels was also seen in a case of chronic alhoholism in a man aged 51.

It should be noted that the perivascular infiltration described above always had to be specially looked for with high magnifications and did not, in any way, even suggest the conditions found in general paralysis, syphilis, trypanosomiasis, etc.

In the spinal cord very similar changes were observed in the vessels and in most cases there was more or less definite increase of connective tissue along the septa. Dilatation of the small vessels in the gray matter of the cord was also striking in some of the cases.

Here it would be well to mention one case, uncomplicated by any disease other than pellagra, in which one of us (L. J. P.) found a number of vessel cells containing a peculiar body which at first glance strongly suggested an intracellular parasite. This body in many respects resembles those described by Borrel in carcinoma, and to a less extent those by Councilman in variola. As is well known, subsequent investigations in both these instances have shown that they represent degenerative products and this would indicate the need for extreme caution in determining, microscopically, the presence of intracellular parasites. As will be seen in the illustrations these bodies have a fairly constant form. They stained purplish-red with thionin and existed only in the vessel cells but in large numbers. It should also be noted that there is no reaction

around the vessels which in any way suggests a local infection. We have been unable to demonstrate them in any other case with any method of fixation or staining and have even failed to find them again in sections from the same blocks of tissue prepared with an apparently identical technique, as those in which they were first seen. We believe them to be either nuclei, sometimes undergoing mitosis or possibly a form of degeneration similar to that described by Schmorl. This last explanation was suggested by Prof. Zeit, of the North Western University, upon examination of the specimens. The former hypothesis seems the more probable for the reasons that the shape is so uniform, and there seem to be such definite mitotic appearances.

Neuroglia—

(a) *Fibers.* In all cases there was more or less increase of glia fibers in the outermost layer of the brain cortex which was especially marked in and about the sulci and around the vessels. In some cases the glia fibers were found invading the pia, causing adhesions between it and the brain. Similar increase of glia fibers was also present in the spinal cord, especially around the periphery and about the central canal.

(b) *Cells.* The *satellite* or *Trabant* cells were increased, more or less in all cases, about those ganglion cells which showed the true Nissl changes, and hence especially about the smaller cells, but this was not observed in the examples of axonal reaction which involved rather the larger elements. The satellitosis was quite definite, and in some cases marked, but nowhere to anything like the degree seen in general paralysis. It has been described by Marinesco, Nissl, Simchowicz and others in connection with states of intoxication of various kinds and seems to represent a mode of reaction upon the part of the glia to toxins which are locally present and directly affecting the nerve cells.

The *glia cells* of the outermost layer of the brain cortex were frequently distorted, shrunken and darkly staining, with metachromatic nodules within the nucleus. The small glia cells of the cortex were moderately increased in numbers, in a few cases forming considerable masses about the vessels. Fatty degeneration of the glia cells was found in all cases. In two cases, one of chronic alcoholism

and the other with septic infection following erysipelas, a few giant glia cells containing two or more nuclei were found.

The *astrocytes* in all cases were definitely increased in number, but not to the degree met with in general paralysis nor so marked as is usually found in senile dementia.

The two most marked were examples of senility and chronic alcoholism. Astrocytes have been especially studied by Cerletti. They apparently represent a means for the removal and transfer of the products of nerve cell metabolism to the vessel sheaths. They are usually, if not always, attached by a large process with a broad foot to the wall of a vessel and it seems probable that the transfer of material, collected through the cell and its other processes, takes place through this insertion-process. They are found to be increased in number and in size under conditions such as senility and chronic disorders presenting marked degeneration of nerve tissue.

Many of the astrocytes in our cases showed granularity of the protoplasm. In seven cases a cystic degeneration, of non-fatty character, was found, similar to that described by Cerletti in cases of pernicious malaria, but also observed in other conditions. In all but one of these seven cases the patients had been either senile or the subjects of chronic alcoholism. All three of the interval cases presented this variety of change and died with infective disease.

Giant astrocytes were found in five of the thirteen cases studied with the special glia stains. Two of them in younger individuals with manic depressive insanity and dementia præcox dying from pellagra, two with chronic alcoholism and one, an interval case dying from chronic tuberculosis eighteen months after the disappearance of all symptoms of pellagra.

The vascular insertion-processes of the astrocytes in 9 of the 13 cases were definitely thickened and in one seemed smaller than usual. This last was an interval case, aged 71, dying from acute pleural and pulmonary tuberculosis. In many instances the insertion processes were bent and twisted.

Ameboid glia cells, both of the astrocyte and small cell type, with homogeneous and granular protoplasm were found in all cases. The small cell types were more frequently found lining the vessels than lying free in the tissues. In one case which had suffered from

erysipelas three weeks before death there were also seen ameboid cells undergoing fatty change, which were not present in any other case. The ameboid glia cell, especially studied by Alzheimer, represents a transformation of the normal glia cells, whereby they become phagocytic and engulf foreign particles and exudates. They are met with only in conditions of acute nervous change of all kinds, such as active stages of general paralysis, status epilepticus, about recent hemorrhages, etc., and are entirely lacking when the disease process becomes stationary, as in remissions of general paralysis, epilepsy apart from recent convulsions, and about old hemorrhages and softenings. Their presence in these cases is therefore readily intelligible, as where the pellagra was not active there were other acute infections.

At this point attention may be directed to the condition of the *central canal of the cord* which was found to be occluded in all cases. Such a condition is probably not abnormal in any adult (Ziehen, Schmaus and others), but it should be noted that, here, there seemed to be a definite proliferation of the glia and ependymal cells, amounting to a central gliosis, and not merely a collection of debris and degenerated epithelial cells, such as are generally found in the normal condition. This is mentioned especially for the reason that it has been emphasized in pellagra by many authors, notably Babes & Sion. Its significance is undetermined.

Nerve Cells—

The changes in the ganglion cells of the nervous system are extremely marked and of great importance. They may be divided for consideration into two groups of which the first or axonal type of reaction seems to be more definitely related to the acute pellagra attack, whereas, the second, or Nissl changes, were found in all cases examined.

Axonal Reactions—

In this condition, which can be produced experimentally by injuries to the axone (Marinesco, van Gebuchten), the cell is swollen and rounded, the nucleus is displaced to the periphery where it may form an actual projection on the surface, or may even be extruded altogether. The tigroid substance has for the most part disappeared from the central portion of the cell, blocks, staining well, being often left around the periphery and especially in the

base of the larger dendrites, a considerable mass being often found around the nucleus. The nucleus is distorted, often oval or reniform, stains more or less uniformly with a pale color and there is a well preserved nucleus rich in chromatin.

There was a marked difference between the cases examined at some interval after the pellagra attack and those in which death occurred during or soon after an acute outbreak. Of the *interval cases* two died eighteen months, and one three and one-half months after the attack. The two former showed practically no axonal change at all, in the last it was present to a much less degree than in the acute cases. In one of the older cases no axonal change was found in the brain or cord even in the Betz cells or in the cells of Clarke's column, and only one anterior born cell, situated in the dorsal region of the cord, presenting this change was found. In the second, many of the Betz cells were entirely healthy, although a few showed a simple central chromatolysis without nuclear displacement. In the cord a few cells in Clarke's column showed typical axonal change as did also some of the cells of the semilunar ganglia of the sympathetic. In the case dying three and one-half months after the subsidence of the pellagrous attack a moderate number of the Betz and large pyramidal cells in the anterior central and para-central convolutions showed axonal change, while most presented a picture of central chromatolysis without displacement of the nucleus. In this case also some cells showed a granulation with homogeneous, non-metachromatic, basophil particles not found in any other cases. This change has been described in acute infective diseases and is possibly related to the tuberculosis which was the cause of death.

In the *recent cases* axonal changes were severe in all, and in many involved practically all the Betz cells and many of the large pyramidal cells of the central convolutions. Similar changes were also found in the ganglion cells of the hippocampus, the dentate nucleus, the central ganglia, and the nuclei of the cranial nerves.

In the cord these changes in the cells of Clarke's column were constant and often extreme, they were present in more or less of the anterior cornual cells in eight of twelve cases, in the posterior cornua in four (in one of these more marked than in the anterior cornua). Similar reactions were found also in the posterior root ganglia and in the cells of the semilunar ganglia of the sympa-

thetic and of Auerbach's plexus in the intestine where these were examined.

It is noteworthy that on the whole the Purkinje cells of the cerebellum were the best preserved cells of the whole brain. Some showed central chromatolysis, but none true axonal change.

The cell showing axonal reaction is, except in very severe degrees, capable of recovery and the above facts would suggest that the change is the result of the condition, whatever it be, which underlies the acute pellagrous outbreak. During the interval the cells again resume, to a greater or less extent, their normal state. This type of reaction also seems to result from an injury to the neurone at a distance from the cell and such an hypothesis is well borne out by the absence of satellitosis about these cells noted above.

Nissl Changes—

Under this heading no distinctions can be drawn between the interval and recent cases. The various types met with may be grouped under the following headings:

Type 1. Cell body shrunken and distorted, but in some cases normal in size, more or less uniform staining, pale in color. Nucleus rich in chromatin.

Type 2. Similar cell bodies with pale nucleus which may be of the same, or lighter, color as that of the cell body and containing granules staining a bluish green with thionin. In some of these the nucleus is lost, with or without the nucleolus.

Type 3. Shrunken, uniformly dark staining cell body and dark nucleus sometimes filling almost the whole cell.

Type 4. Simple chromatolysis. Body normal or a little larger. Nissl granules rarefied and pale or present only as a fine dust. Nucleus approximately normal in staining and position. Nucleolus dark.

Type 5. Shadow cells, a more extreme degree than the last. Nucleus absent. The outline of the cell indistinct.

Type 6. Vacuolated cells. Nucleus present. No Nissl bodies but the cell body shows vacuoles.

All the above types of cell change, with the exception of types 5 and 6, are found in all regions of the cortex in all cases although generally most marked in the central and paracentral convolutions. Either shadow or vacuolated cells were present in all but 4 of 14

cases. Similar changes belonging more especially to type 3 were also found in the cells of the gray matter in the cord, most noticeably in the posterior cornua.

Besides these disturbances special mention must be made of the *pigmentary changes* which were very marked in all cases, including even those of younger age. This pigment was present in all types of cell change, as well as in cells showing normal staining, and formed a very prominent feature in the Betz, large pyramidal and other cells showing axonal changes. The pigment stained black with osmic acid, red with Scharlach and blue with nilblue sulphate. In many of the cells, basophil and fibrinoid granules were present in the nucleus. Pigmentary deposits of fatty character of some degree may be considered as a normal phenomenon and the amount unquestionably increases with advancing age (Marinesco and others). Nevertheless, they have been found in a child of only two years (Pilcz). They are, in general, considered to be the result of a failure to remove all products of metabolism, whether this be due to faulty elimination or excessive production. Some have regarded them as the result of degeneration of the chromatin material of the cell (Babes). There can be no question that in the cases studied here they are of pathological extent, far exceeding the amount in which present even at an advanced age. This change in the nerve cells of pellagrins has been emphasized by many authors, notably Kozowsky.

Fibril Changes—

The neurofibrils were successfully stained in ten of our cases and showed similar changes in all, including the interval cases. The changes found consisted of:

(1) Agglutination.

(2) Fragmentation.

(3) Loss of fibrils (in small cells only, with one exception referred to below).

(4) A peculiar encircling of the nucleus and pigment masses with agglutinated fibrils, not, as far as we are aware, previously described in pellagra.

In only one case (senile dementia of severe grade) were the fibrils found to be absent in large cells. When the fibrils were present they showed the reticular formation usual in senile demen-

tia. This case also showed advanced chronic Nissl changes in the cells, with recticulated protaplasm and extreme fatty pigmentation.

The reports of fibril changes in pellagra are somewhat scanty. Parhon and Papinian report one case in which they found complete loss of fibrils in the large pyramidal and Betz cells. This, as already pointed out, is certainly the exception. The neurofibrils have been the subject of extensive study in recent times (Bielschowsky, Simchowicz, Alzheimer, Fuller and many others), and there is a strong tendency to regard them as of extreme importance in the nervous function of the neuron. If this is correct it seems probable that a complete loss of fibrils must mean a complete loss of function, and most likely an impossibility of recovery in the neuron in question. The clinical study of pellagra would make the presence of this sequence of events, in this disease, at least highly improbable.

It is interesting to note that, in spite of the advanced age of some of the cases, no Redlich-Fischer plaques were found and none of the Alzheimer basket cells were encountered. Three other cases besides the one mentioned above showed senile reticular fibril distribution.

In all cases there was noted a marked paucity of processes in the larger cells which was especially striking in the silver impregnated specimens.

Architecture of the Cortex—

This on the whole was but little disturbed. When present the disturbance consisted mainly of a paucity of cells with but slight distortion of arrangement. It was most marked in the Rolandic region and in the deeper cell layers.

Nerve Fibers—

With the *Marchi stain* the brains showed diffuse scattered degeneration of radial fibres in the cortex, but none was found in the supraradiary of tangential fibers. Nowhere did this form definite bundles.

In the spinal cord a few scattered, degenerated fibers were present in all regions, not in any way systemic, involving perhaps to the greatest extent the posterior columns, and especially the subpial fibers in two cases. The crossed pyramidal tracts did not seem to be more affected than the other regions and in some cases were practically free.

The anterior and posterior roots showed a few degenerated fibers sometimes more marked in the cervical, sometimes in the lumbar region. In two cases the number of blackened fibers was quite marked.

Wolters-Kultschitzky Method.—In the cortex we attach no significance to the fact that in some cases there was poor staining of the tangential and supraradial fibers, for the reason that, in such cases, the amount of staining appeared to depend entirely upon the degree of differentiation. The need for care in interpreting such findings has been emphasized by Binzwanger, Nissl, Alzheimer and others. Apart from this no definite changes were found in the brain. In one case there was considerable defect in staining in the cerebellum which can have no relation to pellagra.

In the cord all cases showed some loss of staining in Goll's column which was situated in most instances in the center of the column bordering the middle line. In a few it extended forward to the commissure and in some back to the posterior surface of the cord when it outlined exactly the whole column. Under a high power the degeneration was seen to affect quite scattered fibers, the majority being well stained, and from its situation it seemed to involve for the most part the endogenous fibers rather than the main ascending tract.

In most cases this change was most marked in the cervical region and might be entirely absent in the lumbar and lower dorsal. In one case it was more marked in the dorsal than the cervical region. In two it extended up to the medulla. In two cases similar pale staining was found in the crossed pyramidal tracts, in three in Lissauer's tract, in one in the lateral basis bundle, and in two in the posterior ground bundles.

The fiber degenerations in pellagra have been studied by numerous authors, notably Tuczek, Marie, Lombroso. The older authors claimed to find definite systemic degeneration, generally a combined postero-lateral sclerosis. Later work, however (Spiller and Anderson, et alia), seems to show clearly that systemic degenerations are certainly exceptional and, as will be seen, in the cases we have studied they are not present.

Amyloid Bodies and Pigment Granules.—An excess of amyloid bodies is present in all cases and has attracted the attention of many writers. In many of our specimens they are present in very large

numbers, both in the brain and in the spinal cord They occur beneath the ependyma, along the vessels, in the thickened glia of the most superficial layers of the cortex and periphery of the spinal cord and also around the central canal. The origin of these bodies has been much discussed. According to the older views they represent degenerated axis cylinders or myelin sheaths (Siegert, Wolf, and others) or glia cells (Obersteiner, Redlich, and others). Obersteiner suggests that they are degenerative products occurring within the glia cell body which are at first surrounded by a layer of fat, and that when the cell undergoes disintegration these bodies are set free and the fatty envelope is dissolved. Recently Alzheimer has suggested that they do not exist in the solid form during life, but are the result of precipitation of certain materials from the tissue juices by the fixing fluids. Their meaning is not by any means clear, but they occur especially in chronic degenerative conditions such as the senium, etc.

The pigmentary degenerations of nerve cells have already been discussed and it is only necessary here to mention the presence of free pigment granules of fatty and fibrinoid nature in the tissues and perivascular lymph spaces in all cases. In five of our cases there were also present granules taking a basic stain. These various granules, specially studied by Alzheimer, are also found in all chronic degenerative conditions.

General Discussion—

The one feature which seems to bear the most definite relation to the acute pellagra attack is the axonal change of particular nerve cells already discussed. With this is probably to be related the scattered Marchi degeneration found throughout the nervous system. This particular picture of widespread axonal chromatolysis with special involvement of the Betz cells and those of Clarke's column has been noted by all workers upon pellagra with modern methods of staining (Marinesco, Babes, Lugaro, Anderson and Spiller, Kozowski and others). As has already been noted by one of us this picture is identical with that described by Meyer as central neuritis. In a personal communication this author assures us that none of his cases presented clinically a picture of pellagra. Attention may also be drawn, in this connection, to the publications upon this syndrome, and upon the cytology of the brain in mental dis-

orders, by Southard, Coriat, Cotton, Somers, Orr and Coles. In a case of chronic alcoholism recently studied by us, there was, clinically and pathologically, a picture of central neuritis and yet nothing to suggest a history of pellagra. As a matter of fact it would be impossible to distinguish microscopically between the specimens of this case and those here described. We must, therefore, conclude that pellagra is not capable of recognition post-mortem, apart from the presence of the typical skin lesions. This is contrary to the opinion expressed by Kozowski in his very detailed report of cases with an excellent digest of the literature. It is of interest here to call attention to an oft-quoted case published by Righetti in which he specifically speaks of polyneuritis in a case of pellagra. The examination concerned only the spinal cord and peripheral nerves, and while the axonal changes in the gray matter and sympathetic system are characteristic there was also a focal hæmatomyelia in the lumbar region with clinical symptoms suggestive of such a lesion. It is even more striking to find that as specifically stated, there was no clinical history of pellagra and the diagnosis was made chiefly upon the grounds that the patient's mother had had pellagra, and she was living under conditions which favor its occurrence.

The interpretation of these facts is possible in only one way, namely, that such a picture as that presented in central neuritis is a mode of reaction to some harmful agent circulating in the blood, acting upon the axis-cylinder processes of the neurons at some point in their course. Further, it seems clear that this change may be brought about by various ultimate causes, although it is conceivable that the actual excitant of the reaction is the same in all and a product of body metabolism under morbid conditions.

Besides these acute changes we have also demonstrated the presence of more chronic nerve cell and glia changes (chronic Nissl change, pigmentary changes, satellitosis and the presence of an increased number of astrocytes, many of which show various forms of change), which indicate the existence of more chronic type of reaction. That this is in an active state at the time of death is shown by the presence of ameboid glia cells. These changes also differ from the axonal reaction in that they suggest a direct, or primary, action upon the nerve cell. It is very difficult to determine the exact relationship of these changes to pellagra, but since they

are apparently constant even in the interval cases (these, however, are not uncomplicated) it seems possible that there is a more chronic degenerative and toxic basis, interrupted at intervals by more acute exacerbations. A study of uncomplicated cases of pellagra dying during a free interval would be necessary in order to throw much light upon this problem.

We do, however, feel justified from the facts here recorded in drawing the conclusions that pellagra is accompanied during the exacerbations by a generalized intoxication and that there is nothing specific in the histologic picture presented.

A few words are also advisable upon the relation to the vascular changes found, for the reason that Kozowski considers them of primary importance. In collecting his material he insisted upon the following requirements: (1) The presence of skin, gastrointestinal, nervous and psychic disturbances; (2) the absence of previous alcoholism, syphilis and bad surroundings; (3) the cases must be under 40-45 years. These conditions must be extremely difficult to fulfill and would exclude many recent attacks in which psychic symptoms might be absent. If he succeeded in regard to the second condition it is certainly extraordinary that so many of his cases should show an extreme cirrhosis of the liver and spleen. He describes the former organ as grating under the knife. In none of his cases does he fail to find hyaline degeneration of arteries in some organs, whereas, even with the advanced age of our cases, we find them in only two. We also have failed to find an *état criblé* or evidences of focal vascular lesion with occlusion of vessels which are so frequent in his series. Either there is a considerable difference in the character of the disease in Bessarabia as compared with that in Illinois or there must be some other factors at work. Kozowsky is supported in his views by the findings of Mariani, in cases not so carefully selected, but negatived by Lukacs and Fabinyi. Such changes cannot therefore be regarded as constant or essential in pellagra.

We have described a small amount of infiltration of the perivascular sheaths of the smaller arteries and wish here to emphasize the fact that we do not regard this in any way as evidence of a local infection. The statements already made with regard to the axonal type of reaction should sufficiently negative this view.

Conclusions—

(1) Pellagra is accompanied by a general intoxication during the acute exacerbations.

(2) In common with other intoxicative conditions pellagra gives rise to a "central neuritis" reaction.

(3) None of the changes are characteristic of this particular form of intoxication.

(4) There is no evidence of a local infection of the nervous system.

SOME FINDINGS IN THE CEREBRO-SPINAL FLUID OF INSANE PELLAGRINS.

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Owing to the similarity of many cases of pellagra to paresis, tabes, etc., Dr. E. M. Green, Clinical Director of the Georgia State Sanitarium, suggested to me that I undertake the examination of the cerebro-spinal fluid of such cases to see if the fluid would show any definite pathological changes similar to those that occur in syphilitic and parasyphilitic diseases of the cord and meninges.

While our findings are not constant and similar in every respect, they are, I think, of sufficient interest to report to this Society, and I hope will stimulate further work along this line which may clear up some of the unknown things about pellagra.

Our work has consisted principally of examining the fluid for increase in cellular elements and protein or albumin constituents, and a *rough* differentiation of those cellular elements found.

The cellular elements of the cerebro-spinal fluid, together with its chemical constituents, have only in the last few years been recognized and studied, and have therefore assumed importance from a diagnostic standpoint, more especially in such diseases as paresis, tabes dorsalis and cerebral-syphilis.

I have examined the fluids from over ninety insane pellagrins, and I feel certain that there are some abnormal or pathological changes occurring in such cases which deserve consideration, and

At present the various methods and technic employed in the which upon further investigation may prove of much value in the examination of cerebro-spinal fluid give almost as many different study of this terrible disease.

results as the number used. This difference is more especially prominent regarding the different types of cells found.

The cellular elements present in pathological fluid show many different characters, and the classification of such cells is at present very much unsettled and lacks entirely uniformity. Even in such diseases as tabes, paresis, etc., where these changes are most marked and more or less constant, there is the same doubt as to the classification of many of the cells found in the fluid, and of

course any classification of such elements in other diseases must to a great extent be a matter of personal choice and technic.

Normal cerebro-spinal fluid contains from 0-5 cells per cb. mm., and any specimen showing 10 cells or over is generally regarded as pathological. Normal fluid also contains a small amount of albumin or protein element, together with other constituents that need not be mentioned here.

In paresis, tabes and cerebral-syphilis and certain forms of meningitis the fluid contains an excess of albumin or serum globulin with large quantities of cells, mostly lymphocytes, varying from 15 or 20 to 500 or more per cb. mm., usual average of 60 to 100 per cb. mm.

In the cases of pellagra here reported upon I found an average of 16.69 cells per cb. mm. and nearly every case showed an increase above normal in the albumin or protein content. Several specimens showed few or no cells, but an increase in the albumin or protein content. A large number of the specimens contained 20, 30 and 40 sells per cb. mm., and as a rule showed a decided increase in the protein content. Sixty-four cells per cb. mm. is the highest number found; that is, where other complications are excluded.

Specimens were examined that contained 55, 60, 72, 80 and 163 cells per cb. mm., but when such complications as tuberculosis, etc., are considered this increase is very doubtful as being due to pellagrous lesions. The specimen containing 163 cells per cb. mm. was from a patient which had received "salvarsan" three or four months previously. This high cell count after the administration of "salvarsan" seems to be somewhat similar to manifestations noticed in syphilis by Ravaut. (See abstract from Presse Medical, J. A. M. A., April 13, 1912, pp. 1156.)

Seventy-four out of eighty-five specimens, or over 87%, gave a positive increase in albumin or protein elements as evidenced by the butyric acid reaction of Nogouchi, which consists of heating .2 cc. of spinal fluid with .5 cc. of a 10% solution of pure butyric acid in normal saline solution, adding .1 cc. of normal sodium hydrate and reheating. A positive reaction is indicated by a floculent or granular precipitate of varying intensity, which gradually settles to the bottom of the tube. There should be no trouble in reading the reaction, as a normal fluid gives no precipitate though it may become slightly cloudy; even a disinct cloudiness should not

be called a positive reaction, and the specimen must be free of blood, as it causes a false reaction to take place. There are other tests that may be used in examining for increase in protein content, but the butyric acid test of Nogouchi is considered the best by the most workers along this line.

Fifty-six out of 90 specimens, or over 62% contained above 10 cells per cb. mm.; this of course does not include those specimens which contained between five and ten cells, and also gave a positive increase in protein or albumin, which would indicate that they were pathological fluids.

The cell counts were for the most part made in a Zappert ruled hæmacytometer after adding a drop or two of Fuchs and Rosenthal's original stain (Methyl violet 0.1, glacial acetic acid 2.0, distilled water 50.0) from a capillary pipette to about 1 cc. of fluid. Two different lots are examined and an average count made from the two.

Differential counts have also been made in many specimens from sediment obtained after centrifugalizing the fluid at a high (3,000 revolutions or over) speed, but I feel that the results are not worth mentioning, except to say that lymphocytes generally predominate, and that the percentage of unknown cells is very high and that the peculiar characters of the latter are entirely too complicated for me to consider until I have obtained more information on the subject.

In the class of cases here reported upon many complications from other diseases are likely to be a contributing cause in increasing the cellular elements and protein content of the cerebro-spinal fluid, but this has been excluded as far as possible, both by clinical and laboratory examinations. Unfortunately I have not been able to do Wassermanns on but eleven cases; three of these were positive, one being from a patient that died twenty-four hours after the blood serum was obtained. In four cases we were able to obtain autopsies, which failed to reveal anything that would indicate syphilitic or tubercular infection of the central nervous system.

The three cases giving a positive Wassermann gave a positive butyric acid reaction also, and contained 55, 7 and 0 cells per cb. mm. respectively.

The eight cases giving a negative Wasserman reaction gave positive butyric acid reactions, and contained 163, 64, 55, 25, 22, 21, 2 and 0 cells per cb. mm. The specimen containing 163 cells is the

same referred to above as having had salvarsan, which possibly accounts for the negative Wassermann, although the case was clinically one of pellagra. In connection with the above cases, showing a negative Wassermann, it is interesting to note that the two cases with 0 and 2 cells each gave a decidedly heavy butyric acid reaction, and that the cases with two cells was a negro male with a severe wet form of pellagra, and who is now apparently convalescing. In fact, the most significant fact in the large majority (87%) of the cases examined is the increase in the protein content of the fluid and that the increase of cellular elements and protein or albumin do not appear to occur in the same specimens as constantly as they do in paresis and tabes. In the latter diseases a heavy butyric acid reaction or protein content almost always means a high cell count; this does not hold good in pellagra. Some of the most typical cases examined gave exceedingly heavy butyric acid reactions with low and even no cell counts, while some specimens gave slight and medium butyric acid reactions with as many as 30 or 40 cells per cb. mm.

The four cases that came to autopsy are reported briefly as follows: No. 486—24 cells per cb. mm., positive butyric acid reaction; revealed at death pachymeningitis, atelectasis, old adhesions in peritoneum, fat necrosis of messentery, chronic interstitial nephritis and a double infection with trichocephalus dispar and strongyloides stercoralis; No. 487—55 cells per cb. mm, positive butyric acid reaction; revealed old meningitis, old adhesive pleurisy and tubercular lesions of right lung. Otherwise there was no gross lesions that would indicate the cause of death. A microscopical examination of the spinal cord showed some atrophy of the ganglion cells in the anterior horns and a few of the cells appeared to have irregular areas of degeneration and displaced neuclei. Case No. 487 is the one already reported as giving a positive Wassermann twenty-four hours before death; No. 508—18 cells per cb. mm., positive butyric acid reaction; revealed edoema of pia atheroma of aorta, adhesions right pleural cavity, and last but not least four large calculi in left kidney and one in the right kidney. This patient had been in the institution for seven months and had apparently improved until about one month and a half before death, when the first attacks of renal colic were noticed. No. 510—42 cells per cb. mm., positive butyric acid reaction;

revealed thickened dura, old pleuritic adhesions, a parenchymatous nephritis and a decided congestion of mucous coats of cæcum and colon.

In concluding I desire to call attention to an article by Boveri in the Presse Medical. According to an abstract from this article in the J. A. M. A., May 18, 1912, pp. 1547, "Boveri found an increase of albumin and a slight lymphocytosis in the cerebro-spinal fluid of pellagrins."

To briefly summarize: A large percentage of the specimens examined showed both an increase in protein content and cellular elements; however, the increase of the former appears to be more marked and more constant. And from the evidence so far obtained it appears that there are definite pathological changes in the cerebro-spinal fluid of insane pellagrins which similate very much the changes found in the fluid of tabetics, paretics and cerebral-syphilitics.

Other than this I have no conclusions or explanation to offer and ask that you consider this a preliminary report, as I hope in the future to clear up many points that at present are unexplainable.

THE EXPERIMENTAL PRODUCTION OF LESIONS RESEMBLING PELLAGRA.

By HERMAN M. ADLER, M. D., Boston Psychopathic Hospital, Boston, Mass.

(From the Laboratory of the Danvers State Hospital.)

In presenting this account of certain observations that were made in the course of experiments conducted during the past three years, it should be understood that it is not my intention to enter the lists for or against any of the present theories of the causation of pellagra. The small number of clinical cases of pellagra that we in the North are given the opportunity of seeing preclude our arriving at any complete conception of this disease. On the other hand, the very fact that cases do occur in the North under conditions which at first sight seem radically different from those which are believed to be predisposing to the occurrence of pellagra should lead us to consider that this disease may be of more general and fundamental importance than is usually conceded.

In the course of the past two years, without any special effort on my part, four cases of pellagra have come to my notice, all inmates of Massachusetts institutions.[1] Undoubtedly, as the interest in this disease is further aroused, more cases will come to our attention. It is clear, then, that pellagra is not without considerable importance for us in the North, as has been pointed out by many authors, and it becomes necessary to inquire into its significance. The question that immediately presents itself is perhaps comparable to the question that is raised by the occurrence of such diseases as pernicious anemia, the results of arteriosclerosis, et cetera, in the insane.

In all diseases we are accustomed to consider two main factors: the one, the causative factor; the other, the reaction of the individual to the causative agent. The importance that has been given to the infectious diseases on account of the remarkable advances in this branch of knowledge during the past decades has, perhaps, diverted the attention of most investigators to a more or less degree from the consideration of the second factor, that of the reaction of the individual to the causative agent. When, however, we under-

take the investigation of the chronic diseases, of which arteriosclerosis and various forms of insanity are perhaps the most striking examples, the importance of the particular causative agent in any individual case is often overshadowed by that of the reaction of the individual. In a case of arteriosclerosis, for instance, it is not enough to discover that the pneumacoccus has infected the lungs and is causing pneumonia, but the all-important point is, what is the individual's reaction to this organism. In one case we may find that the result is a typical, straightforward lobar pneumonia, in another case we may find practically none of the symptoms of lobar pneumonia, but indefinite symptoms and signs of a low grade septic infection running a more or less rapidly fatal course with or without mental symptoms, and offering at no time a clinical picture which can in any sense be called specific for the pneumococcus. It is this point of view which is essential in considering the mechanism of most chronic diseases, and, in my opinion, it is this point of view which is of importance in attempting to determine the clinical significance of pellagra.

In the course of an investigation conducted with the object of determining the reasons for emaciation and anemia in many chronic diseases found among the insane and senile, the following main points have been made.[2]

It has been found that certain cases of emaciation were suffering from the effects of a fat intoxication. This is a condition which has long been the object of attack by pediatricians. While in the realm of infant diseases the main stress has been laid on the intoxications with foreign proteins, there are a number of instances on record where loss of weight, gastrointestinal disturbances and anemia, often approaching the pernicious type, have been observed as the direct effect of intoxication by foreign fat

A similar condition has been shown to exist in certain cases of extreme emaciation due to general paralysis.[3] In these cases it was possible to demonstrate an autohemolysine in the serum after overfeeding with fat in the form of milk or cream. The autohemolysines disappeared regularly when the fats were reduced. These experiments pointed to the existence of a defect in the ability of the individual for handling what under normal conditions was a food. It is an instance of an intoxication by a substance which ordinarily should help rather than harm the organism. The work

of Faust and Tallquist[4] leads us to assume that the hemolysine in this case was oleic acid or some similar chemical substance.

Experiments on the production of pernicious anemia in rabbits by overfeeding with olive oil, cotton-seed oil, chemically pure triolein, etc., have brought out the facts that an excess of fat may be absorbed by the intestines; that, having been absorbed, it will produce at times the symptoms of acute enteritis, loss of weight and in time a varying degree of anemia, which may be severe enough to closely resemble the pernicious type. In these experiments ten rabbits were subjected to chronic poisoning with oil. Of these, three had previously been fed daily for about a year with 0.3 gram of quinine. Three rabbits had been treated for three months with intraveneous injection of 0.01 gram of quinine daily. The remaining four received daily feedings of olive oil without previous treatment. Five cubic centimeters per kilo weight of olive oil was the dose given to all of the rabbits.[5] All of these rabbits developed the blood picture of a secondary anemia within a few days. In four the blood picture of pernicious anemia developed in from two to three months and lasted for a few days. The weight curve followed approximately the appearances in the blood, dropping sharply as the anemia became marked, rising as the anemia improved. The weight and anemia improved markedly whenever the feeding of oil was temporarily suspended.

In six out of these ten rabbits there appeared during the latter part of the experiment, four months or more after oil feeding was commenced, a skin eruption on the inner surface of the ears. This condition was in the nature of a diffuse lesion, characterized by intense congestion and thickening of the entire ear. The ears would become so much thickened that they could be folded over with difficulty and the congestion caused them at times to appear dark purplish in color. This appearance of the ears was invariably accompanied by acute enteric symptoms, profuse diarrhœas and bloody stools. At the same time the weight of the animal dropped rapidly. The oil feedings were discontinued and the symptoms lessened in severity and disappeared. The ears gradually improved until little remained except a few crusts. On feeding oil again, frequently the intestinal symptoms returned, but only in one case has the eruption in the ears increased in severity a second time. Five out of the six rabbits showed the ear lesion during the months

of June, July and August, improving through the fall. One animal showed the ear lesion in May and improved in the course of the summer. The three rabbits that had been fed quinine for a year previous to the oil feedings at no time showed any signs of an eruption or inflammation in the ears. The fourth rabbit that failed to show these symptoms was one of the three that had been treated with the intravenous injection of quinine.

During the entire experiment the animals were kept in all other respects under the same conditions as they had been previously, and under the same conditions and in part in the same cages with control rabbits that were not under experimentation. Not a single rabbit in our entire animal house at Danvers out of some 25 to 30 animals, showed anything resembling this eruption, except the rabbits mentioned. The rabbits were not kept isolated in any sense, and all were fed alike, the same food, in the same amounts, from the same stock. The only difference between the animals under experimentation and those not, lay, so far as could be ascertained, in the feedings of oil.

It would seem that there were several factors involved in the production of this condition. In the first place, we have the introduction of a large amount of oil, the chief constituent of which is triolein. This triolein is split up in the intestine, in part at least, into glycerine and oleic acid, and the oleic acid is absorbed. Oleic acid is a hemolytic agent, and, unless neutralized in some fashion, will cause destruction of red cells. It appeared furthermore from experiments conducted upon the brains of cats[6] that oleic acid is a neurolytic as well as a hemolytic agent; that is, it will destroy by lysis the nerve cell in the same way as it destroys the red blood cell. It is very probable that this lytic action of oleic acid is not confined to these two types of cell.

In the second place, we have to consider here the effect upon the intestine. This seems to be due to the irritating action of the hemolytic oleic acid, probably not only upon the red cell but also upon the smooth muscle coats of the intestine. At autopsy an intestine in this condition shows a marked congestion of the mucosa and submucosa, especially in the region of the lymphoid cells beneath the epithelium of the villi. The cathartic action of olive oil has long been known to the clinician. Its absolute harmlessness in all doses, however, may be doubted in view of these findings.

In the third place, we have to consider the production of a superficial eruption on the skin in one part of the rabbit, namely, the ears. The only immediate reason that I can assign for this site is that it is the only place on the body of a rabbit which is not covered by fur. Attempts to prove this point by shaving parts of the body failed on account of the length of time required for the reaction and the practical difficulties of keeping the animal shaved closely for such a period. This part of the work is at present being repeated. There were at no time in any of these animals any symptoms pointing to an involvement of the central nervous system, nor were any lesions discovered post-mortem.

These experiments seem to be presumptive evidence that a condition which is characterized by a dermatitis and acute enteritis need not be necessarily a clinical entity in the sense of being a specific reaction to a specific causative agent, but that this may be a more or less general reaction common to a large number of pathological conditions. If we assume that the mechanism of this sort of disease includes on the one hand a causative agent of the general nature of the chemical used in these experiments, on the other hand a protective apparatus which has a greater or less degree of strength, we can conceive the production of the same symptoms as a result of considerable variation in the exact mechanism.

In the first place, the causative agent may be so powerful as to overwhelm the protective apparatus of the best equipped individual. This powerful effect need not depend upon quantity. For instance, it is accepted that the hemolytic action of oleic acid depends on the fact that it is unsaturated. Oleic acid, however, contains only one double bond or unsaturated bond in its molecule. There are substances of the general chemical and physical nature of oleic acid which are unsaturated, which contain two or more double bonds in the molecule and which are, therefore, more toxic, more hemolytic, so that the dose required of such a substance may be actually very much smaller than that of oleic acid and still act pharmacologically more powerfully. It is well known that a great variety of such unsaturated fats or fatty acids occur in nature. Such unsaturated fatty acids, which in general are classed with the drying oils or the semi-drying oils, are frequently constituents of our foods, as Mizell[7] and others have pointed out. This is true of the North as

well as of the South, where the butter substitutes are in use in considerable quantities. These facts do not, however, preclude the possibility of the introduction or production of such a substance by means of parasites or bacteria, and thus the reaction would be rather to a chemical substance regardless of where it came from, than to the particular living thing that produced the fat.

On the other hand, we have the other factor of the defense of the organism. It has been shown by Stheeman[8] that the chief defensive apparatus for toxic fats is the lymphoid tissue. This lymphoid tissue is found in the body arranged in the lymph glands and spleen, and distributed through the various organs to a greater or less degree, notably in the submucosa of the intestine. Now, it has been observed that the lymphoid tissue of certain cases of insanity and the lymphoid tissue in senescence is diminished quantitatively. The experiments quoted above, in which hemolytic substances were introduced into the blood stream by overfeeding with fat, were carrid out successfully only in cases in which the emaciation suggested a partial atrophy of the lymphoid tissue.

There is one point which is perhaps of the most striking importance in connection with this disease, namely, the relation of sunlight to the production of the eruption. While my experiments have not yet progressed to the point where I can speak with any degree of certainty upon this matter, I am inclined to the belief that sunlight is merely the exciting irritant, but has nothing to do with producing the condition of irritability in the skin. Instead of an ordinary sunburn, the individual is injured to the extent of inflammation, just as some fair-haired people with little pigment in their skin may suffer from an acute inflammation as a result of a slight exposure to the summer sun, which in a brunette would cause little inconvenience. Just what is the mechanism of the production of this state of irritability remains still to be determined. There is, however, considerable evidence in support of the conception that the same condition which produces congestion and peristalsis in the intestine will predispose the skin to harmful attack by light. I hope that in the near future I may be able to report further on this phase of the problem.

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INTESTINAL PARASITES OF PELLAGRINS AND NON-PELLAGRINS—A COMPARATIVE STUDY.

By ERNEST COOPER, M. D., Pathologist, State Hospital for the Insane, Columbia, S. C.

"Almost any one can have a theory, but unless it is based on facts, it should not receive the endorsement of scientists when there are other theories that explain more acceptably the cause for certain effects." So reads a sentence from a recent criticism[1] of a certain theory concerning the cause of pellagra. Since there are some who would have us believe in a theory that helminths and protozoa have an etiologic relation to pellagra, I have thought it worth while to present the findings in the examination for intestinal infection of 88 pellagrins and 325 nonpellagrins, all being insane.

The clinical material was secured from the white and negro female wards of the State Hospital for the Insane, Columbia, S. C. Usually the specimens examined were the result of a saline purge. The method of examination used was that recommended by Stiles, in which thin smears of feces are spread upon slides and examined microscopically; not less than five slides being used before accepting a negative finding.

The parasitic incidence in order of prevalence was as follows:

	Nonpellagrins.	Pellagrins.
Amebæ	20.00 per cent.	13.63 per cent.
Trichuris trichiura	19.77 per cent.	18.18 per cent.
Necator-americanus	10.77 per cent.	11.36 per cent.
Ascaris lumbricoides	8.00 per cent.	6.81 per cent.
Oxyuris vermicularis	2.46 per cent.	3.40 per cent.
Monads	1.84 per cent.	2.27 per cent.

Infection with strongyloides intestinalis was found in one pellagrin.

At the pellagra conference held in Columbia in 1909 Siler and Nichols[2] presented a paper showing a high percentage of infection with protozoa in pellagrous and nonpellagrous inmates of the Peoria State Hospital, Peoria, Ill. Examination of the water supply for the institution showed a local source of infection in the water pipes. Notwithstanding the polluted water supply of that

institution, there has never developed a case of dysentery or diarrhœa in any of the 300 employees and there are 1,800 to 2,000 inmates who have no diarrhœa the year round (Zeller.)[3]

Dr. Willetts,[4] pathologist to the Georgia State Sanitarium, in examining 500 unselected negro women, 35 of whom were pellagrins, found about 50 per cent. infected with ascaris, trichuris, strongyloides, uncinaria, and hymenolepis; amebæ not being mentioned. In the pellagrous, the infection was higher for strongyloides and uncinaria, but lower for ascaris and trichuris than in the nonpellagrins.

Randolph[5] and Green, reporting conditions in Florida, say that repeated stool examination has failed to reveal the presence of intestinal parasitic infection in pellagrins. Allen,[6] of Charlotte, N. C., observed monads in five of seven pellagrins, warns against confusing amebiasis and pellagra, but believes the latter is often complicated by amebic infection. Somewhat in contrast with these findings, we have J. D. Long's[7] account of the presence of amebæ in 50 of 52 pellagrins, while the late W. B. Young[8] said "Amebæ are found in every case of pellagra at some stage of the disease."

Wherein lies the lack of uniformity in miscroscopic findings? Is it in the variability of the predisposing factors? Among the many factors determining intestinal parasitic infection are: climatic and topographic conditions, occupation, sex, age, race, individual susceptibility and unhygienic influences. It has been observed that the greatest number of infections occur after heavy rains, during warm seasons and in localities approaching sea level. Statistics show that infection is greater in the rural than in the urban population, more frequent in men than in women, and that while the greatest number of infections occur during the third and fourth decades, still they are common in children. The partial immunity of the negro to the enervating and deteriorating influences of some parasitic infections is well illustrated by his resistance to malaria and uncinariasis. Harris[9] and Futcher found that in the United States blacks suffer from amebic dysentery less often than whites. In the Philippines the white race is more frequently attacked than the Malay. Harris has pointed out that amebic dysentery prevails largely among the poor, those badly nourished, and in unhygienic surroundings. Finally there is an individual, as well as racial

resistance, for of many equally exposed, some will escape infection owing to natural or acquired resistance.

In the study of parasitic infection of the diseased, in order to a correct perspective, we should know something of the corresponding infection in the healthy, if it exists. Since the relation of amebæ to pellagra has received considerable attention, let us see something of their incidence in healthy people. Grassi, in 1888, first demonstrated amebæ in stools of normal people. Schaudinn, whose classical work on amebæ appeared in 1903, found that 50 per cent. of healthy farmers in West Prussia and 20 per cent. of people in Berlin harbored amebæ. In 1905, Craig observed the parasite in 65 per cent. of 200 healthy men after a saline purge. Dock found amebæ in only 1 per cent. of 200 healthy people, and Musgrave and Strong in 4 per cent. of healthy individuals.

Nine different amebæ have been described as occurring in the human intestinal tract. Of these we need consider only three, viz.: entameba coli; entameba histolytica, and entameba tetragena. It is the first of these, entameba coli, which is found so frequently and so widespread. With respect to the pathogenicity of this parasite, nearly all investigators are agreed that it is entirely innocuous. Castellani[10] and Chalmers say: "This amebæ is a harmless commensal in the alimentary canal of man." This statement is corroborated by Craig and other investigators. Craig[11] has observed instances in which entameba coli has been present constantly four to six years without the slightest symptoms of dysentery being manifested. Since the parasite is so widespread and is found in such a high percentage of normal people, it is not surprising that it occurs in the stools of many who are ill, no matter what the disease. In such cases, entameba coli has been found in 49 per cent. of over 250 cases examined by Craig. It would seem that the normal intestine is more acceptable to the parasite than that of a person sick, as the incidence of infection is lower in the latter class of patients. It is of great practical as well as scientific importance to recognize the harmless commensal and not subject a patient to a long and disagreeable course of treatment for a parasite he does not harbor. The surprising cures of amebic dysentery, in many instances, are in persons infected with entameba coli and not with a pathogenic organism.

Schaudinn first differentiated entameba histolytica. This ameba is pathogenic to man, is a cause of amebic dysentery, and is probably identical with entameba tetragena. The brilliant research of Schaudinn showed that entameba histolytica is infective only while in the spore form of development. The parasite develops by binary fission, gemmation, and spore formation. Amebic spores are diagnostic of this species, but spores develop only during crises in the life history of the parasites; when conditions for vegetative existence are unfavorable. Amebic dysentery and amebic abscess of the liver have been produced repeatedly in cats, dogs and monkeys, either by rectal injection or by feeding spores of entameba histolytica.

Entameba tetragena was described first by Viereck as pathogenic in 1907. His discovery has been substantiated by Hartmann and Prowazek and also by Craig. To this organism is probably due much of the confusion existing concerning entameba coli and entameba histolytica, for its forms might easily be mistaken as transition forms of these organisms.

Identification of these parasites is often difficult, even with a fresh specimen and a warm stage. All three organisms reproduced by binary fission when conditions are favorable to vegetative existence, but reproduction is different in each under other conditions. We have seen that entameba histolytica then assumes the infective form of spores, while entameba coli becomes encysted—eight daughter amebæ forming in the cyst. Entameba tetragena encysts also, but only four daughter amebæ are found. Caution must be exercised not to mistake the four-daughter stage in the development of entameba coli for the fully developed cyst of entameba tetragena. Doctor Stiles[12] has recently called attention to the simple method of determining the species by studying specimens of stools several days old when these diagnostic forms may be found.

What etiologic relation have investigators proved to exist between amebæ and pellagra? None, other than the occurrence of unidentified amebæ in the stools of pellagrins. Since none of the pathognomonic lesions of entameba histolytica and tetragena have been found in pellagrins at autopsy, and since there is no experimental proof of their presence as etiologic factors, we are justified in concluding that:

The harmless commensal—entameba coli—is the organism so frequently found and that the presence of entameba histolytica and entameba tetragena as complications is accidental.

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ARE SPECIFIC FLUORESCENT SUBSTANCES PRESENT IN THE BLOOD SERUM OF PELLAGRINS?

By ARTHUR D. HIRSCHFELDER, M. D., Associate in Medicine, Johns Hopkins University, Baltimore.[1]

Ever since v. Tappeiner and his pupils have shown that substances which are fluorescent may be inactive when administered to animals kept in the darkness but give rise to skin eruptions when the animals are exposed to the sunlight, there has arisen the interesting question as to what role fluorescent substances, especially those derived from the foodstuffs, may play in the production of various diseases, and particularly those which, like pellagra, are supposed to be associated with the ingestion of certain good or spoiled foodstuffs. This question in pellagra has been rendered all the more interesting on account of some observations made upon buckwheat poisoning in animals. It is well known to veterinarians that cattle or smaller animals fed upon buckwheat develop no symptoms when they are kept in the stall, but when they are exposed to sunlight skin rashes and constitutional symptoms develop. Oehmke has shown that this action of buckwheat is due to the presence of a fluorescent substance in the buckwheat. Since certain analogies between buckwheat poisoning and pellagra have been noted for decades, it seemed worth while to examine the blood serum of patients suffering from pellagra with particular reference to the presence of fluorescent substances.

Since my observations were made Raubitschek has been able to produce skin infiltrations in white mice fed upon good corn and exposed to light, but not in those kept in darkness. He found that the substance responsible for this could be completely extracted with alcohol and was fluorescent.

The estimation of fluorescence is based upon the fact that all fluorescent substances under the influence of light rays give out a light of their own which is of a different wave length and hence of a different color from the light striking them. Thus, quinine sulphate, which is white when one looks through it, appears bluish when held against an opaque object or a black surface. Eosin,

[1]From the laboratory of the Peoria State Hospital, Peoria, Ill., and the Medical Clinic of the Johns Hopkins University.

which is red by transmitted light, has a greenish shimmer by reflected light. This property of fluorescence has been shown by Witt to depend upon certain chemical properties and particularly upon a certain architecture of the molecule. Though possessed by lipochromes, it is relatively rare among substances of the aliphatic series, but relatively common in those with ring structures and particularly in those which contain several benzene rings linked together. It is somewhat greater in those whose rings are united at two of the carbons than in those in which single carbons are united.

It is possible to determine whether a substance is fluorescent in three ways:

1. By placing it in a tube in a dark chamber traversed by a beam of very strong light. If it is fluorescent the path of the beam across the tube will become luminous and emit a light of a color different from the rest of the tube and from that of the light itself.

2. Most of the light rays used in this process may be absorbed by passing the beam through a series of color screens which absorb all except the ultraviolet rays, and when these rays strike the fluorescent substance the path of the ray becomes luminous, although it does not do so if a nonfluorescent substance is placed in its way (Wood).

3. The tube may be viewed against a screen bearing white and black bands, the former showing it by transmitted, the latter reflected light. This simple method is delicate enough to reveal fluorescence in eosin solutions so delicate that the pink color could barely be detected.

In this investigation the first and third methods were used, the source of light being an incandescent lamp whose light was concentrated by means of an Abbé condenser. The tube containing the serum was examined either by placing it in a dark chamber through which the beam of light from the condenser passed or else by looking at it lengthwise against a white cardboard bearing a band blackened with India ink. Both methods showed clearly the fluorescence of extremely dilute quinine sulphate and eosin. By both methods it was perfectly easy to distinguish a definite fluorescence in the serum of three normal patients and five pellagrins in various stages of outspoken and acute pellagra; but it was impos-

sible to distinguish the slightest qualitative or quantitative difference between the normal persons and the pellagrins in this regard.

In conclusion I desire to express my thanks to Dr. George A. Zeller, of Peoria, and to the Illinois Pellagra Commission for the privilege of carrying on these experiments at the Peoria State Hospital, and to Dr. R. H. Winsor for his assistance.

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THE EFFECT OF DIPLODIA ZEAE AND SOME OTHER FUNGI UPON SOME PHOSPHORUS COMPOUNDS OF MAIZE.[1]

By HOWARD S. REED, Plant Pathologist, Virginia Agricultural Experiment Station, Blacksburg, Va.

In a recent paper[2] the writer has called attention to the presence of the fungus, *Diplodia Zeae,* upon maize and to the possibility that this fungus may play a role in the etiology of pellagra. Data were presented showing that following the growth of the fungus a toxic substance was generated which was believed to be similar or identical with the "pellagrozein" of Lombroso. The investigation of protein constituents of mouldy maize is still under way; in the meantime some data have been secured upon the relation of phosphorus compounds of maize.

The idea that spoiled or mouldy maize may contain larger amounts of inorganic constituents would seem to be a logical assumption, since it is well known that the active respiration of the moulds and bacteria oxidizes large amounts of the carbon compounds. Black and Alsberg[3] found, however, that a badly spoiled maize was not always characterized by a high ash content, although in Italy a high ash content is regarded as significant.

The object of this contribution is to bring together some data on the presence and possible significance of inorganic phosphates in maize inoculated with pure cultures of mould fungi, along with some samples of moulded commercial corn.

The fact that a water extract of mouldy maize contained more material precipitable by basic lead acetate than the water extract of sound maize was noted in my earlier work. Following this suggestion an investigation of the phosphorus compounds was in progress when the noteworthy paper of Crawford[4] appeared. His conclusions are that "The chief poisonous principle in certain cottonseed meals is a salt of pyrophosphoric acid. In some this salt seems to be simply one, presumably inorganic, while in others it is more complex, perhaps an organic one."

Without discussing *in extenso* Crawford's work it may be said that he has found no entirely satisfactory way for distinguishing

between the salts of pyrophosphoric acid and salts of other forms of phosphoric acid, but from their chemical and biological effects he regards them as pyrosalts.

Near the same time at which Crawford's paper appeared the work of Forbes[5] was published giving an account of methods of analysis which seemed likely to prove of value in the study of maize and the changes in it due to fungi.

Where this method was used the procedure was as follows: Ten gram samples were extracted with 300 cc. of 0.2 per cent. HCl for three hours in stoppered flasks with frequent shaking. The extracts were easily filtered through dry filters and 250 cc. of each withdrawn and precipitated by the addition of 15 cc. ot magnesia mixture and 15 cc. of strong ammonia. The following day the magnesium precipitate was filtered out and carefully washed on the filter, first with 2.5 per cent. ammonia, then with 95 per cent. alcohol. The inorganic phosphates were separated from this precipitate by extraction overnight in 100 cc. of 95 per cent. alcohol containing 0.2 per cent. of HNO3. After filtration through a dry double filter 75 cc. of the extract was pipetted out and evaporated to moist dryness. The residue was then dissolved in dilute NHO3 and the phosphorus determined gravimetrically in the usual manner.

The acid-alcohol extraction is believed by Forbes to give satisfactory separation of the organic and inorganic phosphorus compounds. After some preliminary studies the following analyses were made, using the methods described by Forbes:

Sample I, weighing 10 grams air-dry, was sound, finely ground maize.

Sample II, weighing 10 grams of air-dry meal, upon which *Diplodia Zeae* had been grown for four months. The meal had been sterilized and inoculated and the fungus grown under pure culture conditions in a cotton plugged bottle. After being air-dried the meal had been ground fine in a porcelain mortar. Both samples of meal were originally taken from the same source.

The analyses made by the above methods gave in sample I inorganic phosphorus calculated as P205 .0192%; in sample II, inorganic phosphorus calculated as P205 0.9488%.[6]

From this analysis it appears that the growth of Diplodia on the meal for four months increased the inorganic phosphorus nearly fifty times. This increased inorganic phosphorus must arise from

the degradation of organic phosphorus and alter by so much the value of the maize for food purposes.

Investigation was also made upon maize meal which had supported a pure culture growth of Diplodia for 14 months. This material was completely blackened by the action of the fungus and had lost considerably in weight. As before the samples were finely ground in a mortar and air-dried. The purpose in this examination was to compare the extract obtained with dilute hydrochloric acid with the extract obtained by the action of pepsin and pancreatin.

Sample V was 50 grams of Diplodia meal digested in 300 cc. of 0.3% HCl.

Sample VI was 50 grams of Diplodia meal digested in 300 cc. of 0.3 HCl containing 0.2 grams pepsin.

Both samples were kept in an incubator at a temperature of 37 degrees C. After 24 hours each sample received 0.5 grams salicylic acid in inhibit the growth of micro-organisms. Sample VI was neutralized with NaOh and then received 0.2 grams pancreatin and 1.0 grams Na2 CO3. Both samples were returned to the incubator for another 24 hour period. After the pancreatin had acted 24 hours both extracts were filtered through paper with washing. The filtrate of each original filtrate was precipitated by adding 50 cc. of strong NH4OH and 50 cc. magnesia mixture. In this case I did not attempt to separate the inorganic phosphorus as in Forbes' method. The magnesia precipitate was filtered out, washed with 2.5% NH4OH then dissolved in 150 cc. of dilute HNO3 and the phosphates determined as pyrophosphate. The results showed the following percentages:

V 0.315 per cent. P205.

VI 0.300 per cent. P205.

The figures show quite close agreement for the two methods of extraction.

While showing considerably less phosphate than Sample II (mouldy meal) analyzed by Forbes' method they are still much greater than Sample I (sound meal).

The other half of the original filtrate from each sample was precipitated with basic lead acetate. Both precipitate and filtrate were treated with H2S and the PbS filtered out. The solutions resulting were evaporated to moist dryness on the steam bath.

After standing for some time the residues were dissolved in water, filtered and used for trials on rabbits. The following were used:

V. The material precipitable by lead acetate.

V. The material not precipitable by lead acetate.

VI. The material precipitable by lead acetate.

The preparations from Sample V were each fed to two different rabbits. That from VI was injected subcutaneously into a rabbit. Each one represented 25 grams of the original substance No bad effects were apparent in any of the rabbits. It has been found, however, by Sturli and others that rabbits are not as susceptible to mould poisons as other animals, *e. g.*, mice, therefore it cannot be positively stated that these products are altogether non-toxic.

Waiving for the present the question of toxic organic substances in moulded meal experiments were carried farther upon the increase in inorganic phosphates. Whether or not the fungus is a factor in the actiology of pellagra, there are deep seated biochemical changes wrought by the fungus infection. As the fungus grows it consumes much of the organic material in respiration. The extent to which this loss may occur is shown by the figures in Table I, which were collected during the progress of the work.

TABLE I, SHOWING LOSS OF WEIGHT IN CORN MEAL INFECTED WITH DIPLODIA ZEAE.

No.		Time.	Per Cent. of Original Weight Lost.
1	Sterilized corn meal control	56 days	4
2	Infected corn meal	56 days	29
3	Infected corn meal	92 days	47
4	Infected corn meal	200 days	55
5	Infected corn meal	200 days	60

From these figures it will be quite apparent that there was a great loss in the food value of the meal due to the combustion of organic compounds by the fungus.

TABLE II, SHOWING SAMPLES, METHODS OF ANALYSIS AND PERCENTAGE OF P2O5 IN SAMPLES OF CORN MEAL.

No.	Source	Method of Analysis	Per Cent. P_2O_5
A	Comm'l air dry corn meal	Forbes	0.0192
B	Diplodia meal, 4 months old	Forbes	0.9488
C	Diplodia meal, 14 months old	0.3% HCl	0.315
D	Diplodia meal, 14 months old	Pepsin-pancreatin	0.300
E	Sterilized corn meal	Forbes	0.118
F	Diplodia meal, 56 days old	Forbes	0.215
G	Diplodia meal, 92 days old	Forbes	0.249
H	Aspergillus meal, 92 days old	Forbes	0.255
I	Mouldy corn (top of cargo)	Forbes	0.1224
J	Mouldy corn (20-50 cm. deep)	Forbes	0.0474

A continuation of the chemical studies with another set of samples showed the effect of fungi in increasing the amounts of inorganic phosphates. In Table II these facts are briefly portrayed.

Samples A and B should be considered together. The analysis of the former represents the phosphorus of a mill sample of corn meal; that of B represents the same after having been wet and sterilized and used as a culture medium four months.

Samples C and D were from another culture on corn meal. The principal object in making their analysis was to get a comparison of the amounts of phosphoric acid extracted by hydrochloric acid and by digestion with pepsin and pancreatin. As shown in the table the differences were not material.

Sample E showed much more inorganic phosphorus than A. This may be referred to two conditions, first, a different sample of corn meal was used, and, second, the meal was moistened, sterilized in the autoclave, and kept for 56 days.

Samples F and G show an increased amount of inorganic phosphorus in comparison with E, which was from the same sample of meal and treated similarly except for inoculation with Diplodia. The culture 92 days old had apparently liberated somewhat more inorganic phosphorus than the culture analyzed at the end of the 56th day.

Sample H was from a 92-day corn meal culture of *Aspergillus fumigatus* obtained from the laboratory of Parke Davis & Company. The analysis shows that about the same amount of inorganic

phosphorus was here liberated as in the case of the 92-day Diplodia culture. The comparison is not without interest since many observers have implicated *A. fumigatus* with the etiology of pellagra.

The analysis of samples I and J possess peculiar interest because they are samples of mouldy commercial corn. They were obtained through the kindness of Dr. J. W. T. Duvel, of the Department of Agriculture. They were taken from a car of spoiled corn which had been about three weeks in transit (November 29th to December 22d). When the car was opened the surface layers had a temperature of 62° C. and every grain was badly infected with a variety of mould fungi, among which species of Aspergillus and Penicillum could be recognized. Sample J, taken from 20 to 50 cm. below the surface was subjected to anærobic conditions and was not infected with the moulds which grew in the upper layers. The lower layers were nevertheless subjected to heating. The grains were dull mahogany in color and quite brittle.

Unfortunately there was no uninfected sample of maize to serve as a control, but an idea of the chemical changes wrought by the moulds may be gained by comparing the inorganic phosphorus content of the two samples. Sample J was clearly not infected with moulds, whatever organisms of an anærobic character may have been present. In sample I the inorganic phosphorus content is between two and three times as great as in the less mouldy sample J.

It is entirely possible that the mould fungi might absorb these inorganic phosphorus compounds and use them in their own metabolism, in which case these compounds would seem to disappear with further lapse of time. The analyses of samples B, C, and D would suggest such a condition. The culture, after 14 months' growth, contained about one-third as much inorganic phosphorus as those which were four months old. It seems quite possible that the increased growth of the fungus and the process of forming spores would use a part, at least, of the inorganic phosphorus liberated by the fungus. The metabolism of the fungus would in that event convert the phosphorus into organic compounds characteristic for that particular fungus. In this connection, it seems worth while to consider the possible formation of some specific substance and their pharmacological effect. Especially would this be important in regard to the formation of organic phosphorus compounds sensitive to light. It is well known that the lesions and

erythemata of pellagra appear almost entirely upon portions of the skin exposed to light. The assumption might logically be made that there is some substance in the body of the pellagrin which is photo-sensitive and when acted upon produce the local effects so characteristic of pellagra. This substance might be supposed to be derived from the action of the mould fungi upon maize.

From the foregoing data it would appear that *Diplodia Zeae* and other fungi grown upon corn meal liberate material amounts of inorganic forms.

Corn meal infected with Diplodia losses in weight; the loss increasing with the age of the culture.

Aside from the question of the possible toxicity of any of the inorganic phosphates thus liberated or their possible role in the etiology of pellagra the data show what is interpreted as a marked deterioration in the food value of the maize, due to the degradation of organic phosphorus and other compounds. As the fungi continue to grow they may take up a portion of the inorganic phosphates, possibly to form bodies having toxic properties.

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[6]It gives me pleasure to acknowledge the assistance of Dr. W. B. Ellett in all this work, and especially in the phosphorus determinations.

V. Clinical Features of Pellagra

EARLY AND UNDEVELOPED CASES OF PELLAGRA.

By Beverley R. Tucker, M. D., Professor of Neurology and Psychiatry, Medical College of Virginia; Neurologist to the City Hospital, Johnston-Willis Sanatorium and Memorial Hospital, Richmond, Va.

I have stated before that *pellagra sine pellagra* could not be diagnosed, that patients frequently have nervous and gastrointestinal symptoms from other causes and that until the cutaneous symptoms develop we should not and could not make a diagnosis of pellagra. I wish now to modify these statements in view of further knowledge of the disease and greater experience with it.

Unfortunatly, we have no laboratory tests to confirm the diagnosis of pellagra before the cutaneous manifestations, as we have, for instance, in typhoid fever where the blood culture and Widal test may be positive before typical clinical symptoms, or in tuberculosis where a radiograph, tuberculin test or sputum examination may be the means of diagnosis before the cough makes its appearance; or in locomotor ataxia where the condition may be diagnosed with few symptoms and confirmed by a high lymphocyte count in the cerebral-spinal fluid or a positive Wassermann or Noguchi reaction. On the other hand, an experienced physician may make a tentative diagnosis of typhoid in the early stage by the history of the probable source of infection, very slight febrile and pulse changes with malaise and headache; an astute diagnostician may make a diagnosis of tuberculosis before the cough appears by history of exposure, silght evening rise of temperature, dilated pupils, debility, slight respiratory and other changes. A good neurologist can usually make a diagnosis of tabes in what is called the preataxic stage by the history of syphilitic infection and slight changes in reflexes or of station and pains of a darting character. These physicians to whom we refer, men of observation and training in their special line, have accurately made the diagnosis of these diseases entirely from early clinical manifestations before the laboratory aids were discovered and now it behooves the pellagrologist

to at times make a clinical diagnosis of pellagra in cases with very slight or possibly without one or the other of the cutaneous, gastro-intestinal or nervous and mental manifestations. We advise nothing radical, but pellagra should be excluded in every case which presents any one of these sets of symptoms.

You will note that I have said I wished to modify, not retract, former statements as to *pellagra sine pellagra*. To make this position clear allow me to say that whereas it may be possible, still it is certainly of exceptionally rare occurrence, that a case of pellagra is seen without cutaneous manifestations at some stage of the disease. On the other hand, it is not uncommon for us to see cases in a precutaneous stage or cases where cutaneous manifestations have been extremely slight and where desquamation has taken place and left the site of the lesion in a practically normal condition. There are also certain cases in which the skin lesions are slight, which have no marked gastrointestinal or nervous and mental manifestations. In other words, very mild cases. I think too much stress has been laid upon marked symptoms and not enough upon slight ones. For example, one may inquire diligently into the history for diarrhœa and find that the patient has not had it, but further search may reveal mild stomatitis, slight salivation, slight nausea and perhaps losseness of the regular actions and slight proctitis. Symptoms of ataxia and change of reflexes may be entirely absent and still the patient may have moderate insomnia, slight vertigo and mild apprehension. The patient may not be objectively insane, but again apprehension may be present, the patient may have become somewhat depressed or even mild delusionary, hallucinatory and suicidal tendencies may be found upon close and careful mental examination.

In regard to the general symptoms, marked loss of weight, debility and anemia may be present or these symptoms may be very slight. It often occurs that we see a patient with a mild case of pellagra in which we are possibly uncertain as to diagnosis. Upon stating the case the patient may say that this is his first illness of a similar nature, but careful questioning of the patient and the family will frequently bring out the fact heretofore ignored, that similar manifestations occurred the previous year and possibly for several years previous. It is needless to say that such a history aids most essentially in confirming the diagnosis.

The usual order of systemic manifestations of pellagra are, first, gastrointestinal symptoms; second, cutaneous manifestations, and, third, nervous and mental symptoms. This order, however, may be changed in many ways and I have seen cases in which the nervous and mental symptoms appeared first and cases in which the cutaneous symptoms appeared first.

As far as treatment is concerned, by far the most useful remedy in my hands has been urotropin. I have used it in the treatment of about fifty cases and find that early and mild cases respond very rapidly and that even severe cases frequently begin to improve within a few days and go into a remission within a few weeks. In some cases the symptoms have recurred the following year and again yielded to the administration of urotropin. In a few cases no recurrence has taken place, one case not having recurred since 1909. I believe this drug to be almost specific in doses of ten or fifteen grains four times a day, provided it is administered in the early stages of the disease.

In the consideration of doubtful cases we shall have to bear in mind the section of the country in which the disease occurs, the diet and general health of the patient, whether there are other cases in the locality, the season of the appearance of symptoms, the history of disturbance of a similar nature the previous year and note carefully such symptoms as stomatitis, salivation, nausea, vomiting, diarrhœa, proctitis, all cutaneous manifestations, especially accompanied by desquamation over the usual sites and the symmetry of these lesions; also whether there is apprehension with mild depression, vertigo, insomnia, change in reflexes, loss of weight, malaise and more or less secondary anemia. A case presenting the majority of these symptoms, however slight, is probably a case of pellagra. If the symptoms arrange themselves so that the gastrointestinal tract, the cutaneous sites and the nervous and mental spheres are involved the diagnosis is confirmed. The writer feels convinced that thousands of mild cases are at present unrecognized and that these mild cases are very amenable to treatment and that some cases remain mild in type while others develop into very severe and marked cases. It is with a view of calling the attention of the profession in a general and discoursive manner to the slight or undeveloped cases which are so frequently unrecognized and unsuspected that this paper is written.

The photographs of the hand presented in the accompanying illustrations were taken of the palmar and dorsal surface of the right hand of a patient during a remission. This patient had a severe case of pellagra two years ago which went into a remission under the administration of urotropin and has not had cutaneous symptoms since. She had, however, last spring a slight gastro-intestinal disturbance and some insomnia and nervousness, but immediately began taking urotropin again which apparently cleared up the condition in a short while. It will be noted that the back of the hand is practically lesion free. The palmar surface is rough, due, not to pellagra, but to hard manual labor. This case illustrates the fact that unless the previous history of a pellagrous attack had been taken one would hardly have been able to make the diagnosis of pellagra last spring when the gastrointestinal and nervous symptoms recurred, but knowing the previous history one could treat the case as a definite case of pellagra even with the cutaneous symptoms absent.

THE ANALOGIES OF PELLAGRA AND THE MOSQUITO.

By STEWART R. ROBERTS, S. M., M. D., Professor of Medicine, Atlanta Medical College, Atlanta, Ga.; Physician to the Wesley Memorial Hospital.

With the publication of Sambon's "Progress Report" in 1910, the investigation of pellagra really began. Before that time men studied a cereal, and thought they were studying a disease. Sambon's name will be associated with two great propositions concerning the nature and cause of pellagra.

1. The hypothesis that it is an infectious disease.
2. The hypothesis that it is an insect borne disease.

To many students these hypotheses stand as facts, because supported by much evidence and therefore believed; to others they are only hypotheses, and therefore only theories, because unproved. The third idea advanced by Sambon, viz.: that the Simulium fly is the specific insect carrier, is open to far larger doubt than his first two propositions; and reasoning by analogy, and by the analogies of etiology, and by many notable comparisons, it is not nearly so apt to be the insect agent as is the mosquito.

The following objections hold against the Simulium as the disease carrier:

1. So far as is known, the bite of the Simulium is poisonous rather than infectious; bearing toxins rather than parasites.

2. The disease appears in America chiefly in those who are not field laborers, and who are little exposed to its bite. Pellagra occurs in sporadic cases in cities, among women who stay at home, and in asylums within doors, where the Simulium neither comes nor bites.

3. It does not present the regularity of seasonal incidence, adults living through the winter, the repeated broods during the spring, summer and autumn, the enormous numbers as does the mosquito.

4. It does not move in swarms far from its stream home, and, therefore, does not explain those cases arising far from any running stream.

5. It is more numerous in cold countries and on the coast of all continents, while pellagra avoids cold climates and seeks the interior rather than the coast.

The insect which carries the pellagrous parasite must account for and explain the following ecological and geographical facts of the disease.

1. Its seasonal relations, its periodicity, its recurrences, and its chronicity.

2. Its endemic relations, its occurrence chiefly in rural environments, its absence from cities except in sporadic cases.

3. Its peculiar geographical distribution over the world, in Africa along the Nile, in southern Europe, southern North America and the West Indies.

4. Its predominance among females, and in those who work around the house, as in women who wash clothes near the home.

5. Its attack on all ages and both sexes, infants, adults and octogenarians.

6. The spread of the disease in new areas, its epidemics and their variations in severity.

7. The severity of the disease in its first sweep of a new era, as in Roumania and America; and the increasing immunity to the disease in Spain and Italy, where it has raged for two centuries.

8. Its association with mosquito borne diseases.

9. Its association with streams, swamps, foothills, valleys, lowlands, and standing water in damp areas.

The following analogies of etiology and comparisons with mosquito borne diseases show a relationship to a common insect host, the mosquito:

1. Pellagrins are insane, become inmates of asylums, and insane inmates conversely become pellagrous, as in the Alabama epidemic reported by Searcy, the Illinois asylum cases reported by Zellar, the Jamaica cases reported by Williams. The two sexes are more equally affected in those who develop the disease within the asylums, and within doors both sexes are equally exposed to the infecting agent. The insect probably lives and bites in houses.

2. The predominance in Italy, Roumania, and America of female pellagrins, and of those of both sexes remaining in and around the home during the day. They are more exposed than those away from home working in the fields or woods.

3. The mosquito accounts for the fact that a woman in the family may become pellagrous, and other women in the same house develop the disease. They are together day and night equally

exposed to the infecting agents. On account of this spread of the disease in one family, under one roof, chiefly among women and children, it has in certain endemic areas been considered contagious, as was yellow fever before the stegomyia fasciata was discovered to be the agent in its distribution.

4. For pellagra to appear in the United States either the parasite, or both parasite and insect host, must have been lately introduced. For it to spread the parasite must be naturally fitted to the climate, seasons, and to insect and human hosts; the insect host must be adapted to climate, seasons, habitat, and environment. For such adaptation to exist on the part of the insect, it must have been in America many centuries and in enormous numbers. The parasite of pellagra has, therefore, probably been recently introduced, and its specific insect host is a natural, long-time, inhabitant and in enormous numbers, as is the mosquito. For instance, Stegoymia fasciata was found in Milledgeville, Ga., in September, 1912, in a soft drink stand, but the yellow fever agent was lacking, and there was no yellow fever in the city.

5. Like malaria and filariasis, pellagra is chiefly rural. Rome escapes malaria, and yet in the marshes without the city the disease rages. Bucharest, Milan and Atlanta escape pellagra, but in the regions round about, the disease persists. Even in large cities where sporadic cases of malaria and pellagra develop, they usually occur on the outskirts where the drainage is poor and filth and sewerage abound.

6. Pellagra has an unquestioned relation to streams, swamp areas, standing water, and places that breed the mosquito, as have malaria and yellow fever. This is true in Egypt along the Nile, and Greece, Roumania, Italy, Spain and America.

7. Hills tend to escape in areas visited by pellagra, malaria, yellow fever and filariasis.

8. In areas both malarial and pellagrous, rains and floods that increase malaria, increase pellagra also. With the drainage of an area both malarial and pellagrous, both diseases decrease and later disappear, as illustrated by the Landes in Southern France.

9. Mosquito borne diseases have a seasonal incidence. Yellow fever in spring, summer and autumn; malarial in spring, summer and autumn; pellagra in spring, summer and autumn. Yellow fever depends in its endemic areas upon the time of the appearance

of the Stegomyia; malaria upon the Anopheles; pellagra upon its specific mosquito host. The first attack of pellagra may develop from early spring to fall, for the reason that several broods of the mosquito host appear during this period.

10. Malaria, yellow fever, filaraisis and pellagra tend to appear and become epidemic with spring and early summer. Within the bounds of latitude, the outbreak of these diseases is later in the spring and summer as one goes farther north, and earlier as one goes farther south. The annual pellagrous attack tends to be earlier the second summer, and the earlier the spring season, the sooner the attack; as is also true of malaria.

11. Pellagra appears and persists in cotton mill communities in the South, and is absent from cotton mill and factory communities in the Eastern States. There is probably an infected mosquito in the South which is absent from the East. The usual factory reservoir. the puddles of water, the surface closets, the washtubs in every backyard, the rain barrels, the mosquito breeding areas, the women at home, are all consistent with the mosquito as a reasonable hypothesis.

12. Malaria, yellow fever, filariasis and pellagra all tend to cease spreading, cases improve, the disease dies away with the coming frost, cold and winter. All these diseases avoid the winter because of the influence of the cold season upon both parasite and insect.

13. Pellagra, like malaria, yellow fever, filariasis and dengue fever, has its epidemics, its years of severity and mildness, its ebb and its flow of prevalence and of intensity.

14. Pellegra, malaria, yellow fever and filariasis are all endemic in restricted areas for a century, and epidemic at different times. These endemic areas are mosquito breeding areas, and in times of epidemic mosquitoes are present in great numbers.

15. Pellagra and malaria have latent periods and periods of activity, due to the change in the seasons, the fixed life period of the parasite, and its alternating periods of activity and rest; and to changes in climate, altitude, and vitality. Spring may usher in an attack of malaria or of pellagra. A surgical operation or a confinement may float a latent pellagra or a latent malaria.

16. Pellagra, malaria, yellow fever and filariasis are noncontagious and noninheritable.

17. The incubation period in malaria is ten days to three weeks; in yellow fever thirty-six hours to fourteen days; in pellagra probably two to three weeks, certainly less than four weeks. Sambon recently found pellagra in an infant one month old. This fact signifies kinship of insect carriers.

18. The parasites that cause malaria, yellow fever, and filariasis, are more restricted in their endemic areas and in their geographical distribution, than their insect hosts; Anopheles has a wider distribution than the Plasmodium malariæ; Cules fatigans than the Filaria bancrofti; and Stegomyia fasciata than the yellow fever agent. The same relational distribution of parasite and mosquito probably applies to pellagra.

19. Pellagra is absent from Ireland, where Simulium flies occur in abundance, but mosquitoes are relatively scarce. Malaria, yellow fever, filariasis and dengue fever are also absent from Ireland. Furthermore, the poorest Irish peasants, whose poverty is famed and world-wide, eat Irish potatoes and "yellow meal," the last imported as shelled corn from America, Africa, and Russia through the Baltic Sea, and yet there is no pellagra in Ireland.

20. Scotland,[1] practically all of England, and Australia are free from pellagra, malaria, filariasis, and yellow fever. Canada is likewise free from all these diseases, except a small area on the shore of Lake Ontario, where a few malarial cases occur. Except for Illinois, where five hundred cases of pellagra have occurred, and a few sporadic cases in the northern and western United States, pellagra, malaria and yellow fever all tend to remain in the southern United States and farther southward. A further significant fact is that the Illinois cases are chiefly asylum cases.

21. Practically all pellagrous areas are also malarial areas, except in the small island of Barbadoes in the West Indies, where pellagra, yellow fever, and filariasis occur, but no malaria. On the near-by island of Jamaica, however, all four diseases exist, pellagra, malaria, yellow fever, filariasis. Pellagra is to Italy and Roumania what yellow fever is to the West Indies, and what malaria is to Greece and to the foothills of the Himalayas in India.

22. Pellagra extends from eight to forty-five degrees north latitude; forty degrees north latitude cuts the pellagrous area of Europe into northern and southern halves, and forty-five degrees marks its

[1]Sambon thinks pellagra exists in Scotland.

northern limit; thirty degrees north latitude cuts the pellagrous area of Africa; and thirty degrees north latitude cuts the North American area, with eight degrees in Panama as the southern and forty-five degrees in New York as the northern limit even in sporadic cases. The distribution of pellagra in three continents is marked by an average latitude of thirty to forty-five degrees, and 90% of the pellagra cases in the world occur in this belt of 15 degrees, or a distance of 1,000 miles from north to south.

23. In this belt occur also malaria, yellow fever, filariasis, dengue fever—all the mosquito borne diseases. Furthermore, while Anopheles occurs in this area, the northern distribution of pellagra generally marks the northern limit of Stegomyia fasciata, and the household mosquito, Culex fatigans. In pellagrous territory in three continents are these three mosquitoes. If the Simulium were the insect carrier, we should expect pellagra in northern as well as southern Europe, in Ireland as well as in Italy, in Minnesota and Canada as well as in Georgia and Panama.

Returning now to the ecological and geographical facts of the disease, the mosquito accounts for its seasonal relations, periodicity, and recurrences; its endemic relations, rural habitat, and sporadic appearances in cities; its peculiar geographical situation in Africa, Europe and America; its predominance among females and those who stay much at home; its attack on all ages and both sexes; the spread of the disease in new areas; its first sweep of severity in such areas and later its gradual decrease and the relative immunity of the inhabitants; its presence along streams, and in mosquito breeding areas.

Whether a single species of the Culicidæ harbors the pellagrous parasite, as in yellow fever, or more than one as in malaria, and what this particular species may be, is a question for the future. It will probably prove to be a rural-breeding, house-living, day-biting mosquito. To us and perhaps to those who shall come after us the problem remains—the investigations, the experiments, and the proof.

ETIOLOGIC FACTORS AND RECURRENT ATTACKS OF PELLAGRA.

By GEO. C. MIZELL, Formerly Associate Professor of Physiology and Gastroenterology, Atlanta College of Physicians and Surgeons, Gastroenterologist to Wesley Hospital and Georgian Hospital, Atlanta, Ga.

At the present time a diagnosis of pellagra is based wholly upon clinical features. The clinical features are not always constant, hence in the state of our present knowledge it is often difficult to say where the pellagrous process begins or where it ends. In view of these facts the term, recurrent attacks, used in this paper calls for some qualification. It appears to be the custom to consider the dermatitis as the one characteristic symptom, and if error is to be avoided a diagnosis should not be made without its presence.

In observing the course of the disease it would be fair to presume that a case going through the summer in fair health, without developing the dermatitis when exposed to the sun is no longer a pellagrin. Likewise it is to be concluded that a case developing the dermatitis under the same conditions is a pellagrin.

Because of the diagnostic significance of the dermatitis this symptom is used as an index to the state of the patients, *i. e.,* when a given case has had an annual recurrence of the dermatitis this is termed a recurrent attack of the disease, or if a case goes through the year without dermatitis it is held that he has not had a recurrence.

In doing this we will not lose sight of the probability that pellagra is a chronic diseases, characterized by peculiar exacerbations due to climatic and other influences.

Thus, in speaking of attacks, we mean an incident which always denotes the presence of the disease, yet there are probably cases in which this characteristic lesion never occurs.

The etiologic features that will be discussed are corn and cottonseed oil consumption, and incidentally age, sex, residence and season. These factors as they appear in one hundred cases will be the basis for our remarks.

By referring to the table it will be observed that the oil and corn consumers who had no attack in 1912 are placed first. Below

these are placed the cases who had attacks in 1912 except case number 100, which is placed alone at the bottom of the table.

After making this division, the cases are further divided into groups according to the consumption of corn and cottonseed oil.

Group I is composed of thirty-three cases, who until 1912 had been having attacks of pellagra for one, two, three or more years. Nothwithstanding the fact that they ate corn products continuously they did not have an attack in 1912. It is also to be noted that these patients, with few exceptions, enjoyed good health in 1912.

In Group II we have twenty-six cases who discontinued corn consumption for some months and had no recurrence in 1912. It will be pointed out later that both of these groups, consisting of fifty-nine cases, together with three cases of Group III, made important changes in diet other than changes in corn consumption.

In Group III are six cases who never ate corn products. These six cases have had a total number of twelve attacks. The first three made changes in their diet at the time of the first attack and did not have a recurrence. The last three did not make any changes and continued to have recurrent attacks. Case number sixty-three had attacks for five successive years.

The cases of Group IV, sixteen in number, suspended corn products and had a recurrence one or two years thereafter.

Group V, composed of eighteen cases, continued the use of corn products and have had a recurrence every year since the first attack.

Summing up the relationship of corn consumption to recurrent attacks we have:

Fifty-one cases continued corn—thirty-three had no attacks in 1912; eighteen had attacks in 1912.

Forty-two cases discontinued corn—twenty-six had no attacks in 1912; sixteen had attacks in 1912.

Seven cases ate no corn—had a total of thirteen attacks.

The table shows that all of the one hundred cases were consumers of cottonseed oil products except case Number 100. Some effort has been made to show how long the oil had been consumed when the first attack occurred. The figures in the table represent the number of years the patients stated that they had been using this food when they developed pellagra. Where this time could not be fixed the number of years is left blank. The annual con-

FIGURE I.—FEBRUARY 7, 1912.

Group I. Corn Consumption Continuous. No Continuation of Recurrent Attacks of Pellagra

FIGURE I.—FEBRUARY 7, 1912.

Group I. Corn Consumption Continuous. No Continuation of Recurrent Attacks of Pellagra.

Our position in regard to this factor is based upon such observations and may be stated as follows: Corn, by virtue of the high percentage of fat and the nature of this fat, may possibly be capable of producing pellagra if consumed for a long time to the exclusion of fats. It is probably true that both sound corn and spoiled corn are equally effective in producing the disease, except that in the case of spoiled corn there are present other injurious products which predispose to an attack of illness through their effect on the general health. The facts set forth in the table show that corn as it is consumed in Georgia, South Carolina and Alabama, has no etiologic connection with pellagra. If it is consumed in sufficient quantity anywhere, either sound or spoiled, the fact remains that the specific agent has not been identified, and that it is not the only cause. Sound and spoiled corn should be withheld from the pellagrin because it contains a fat which is injurious to him while he is so affected.

Before entering into the discussion of the several facts setting forth the relationship of cottonseed oil to pellagra, it will aid us in interpreting these facts to state the theory of the connection.

It is proposed (1st) that when linolin (the characteristic fat of the cottonseed oil group) predominates in the fatty food of an individual it is deposited in the tissues as linolin and as linolyl compounds.

(2d) That linolin and linolyl compounds, by virtue of their unstable nature, readily undergo oxidation in marked contrast to olein, palmitin and stearin, which are among the most stable organic compounds in the animal body.

(3d) That fat and fatty tissue containing linolin and linolyl compounds in excess are unfit for performing the functions designed for normal animal fatty tissue.

(4th) That the end products of oxidation in the case of linolin are different from those of olein, palmitin and stearin.

Of course cottonseed oil can only be connected historically with the present day pellagra. It will not account for the disease two hundred years ago, but there is reason to believe that oils, or seed containing oil, of the same class have been eaten for centuries in pellagrous regions.

A partial list of the suspected oils is given below.

FIGURE II.—FEBRUARY 7, 1912.

OILS CONTAINING LINOLIN IN NOTABLE PER CENT.

Pumpkin Seed Oil.

French—Huile de courage, huile de potiron.
German—Kurbissaninol, Kurbiskernol.
Italian—Olio di pucac.

Maise Oil, Corn Oil.

French—Huile de maise.
German—Maisol.
Italian—Olio de mais, Olio di granturco.

Kapok Oil.

'rench—Huile de kapok.
German—Kapokol.
Italian—Olio di kapok.

Cotton Seed Oil.

French—Huile de coton.
German—Baumwollsamenol Cottonol.
Italian—Olio di cotone.

Sesame Oil, Beniseed Oil, Gingelli Oil, Teel Oil.

French—Huile de sesame.
German—Sesaaamol.
Italian—Olio di sesamo.

Brazil Nut Oil.

French—Huile de noix de Braasil.
German—Paranussal.
Italian—Olio di noci del Brasile.

Poppy Seed Oil.

French—Huile d'oeillette, Huile de pavot.
German—Mohaul.
Italian—Olio di papavero.

Sunflower Oil.

French—Huile de tournesol.
German—Souneufluemerol.
Italian—Olio di girasole.

Walnut Oil, Nut Oil.

French—Huile de noix.
German—Nussol, Wallunssol.
Italian—Olio di noce.

The only point that can be raised in opposition to either of the four propositions is in regard to the adaptability of linolin as a substitute for olein, palmatin and stearin in animal tissue. The difference in the chemical and physical properties of these fats seems to settle this question.

Bear in mind that this theory does not postulate the action of the neutral fat linolin as being a poisonous or toxic agent upon its entrance into the body, but that it gradually accumulates in the absence of other fatty food, and when it is in excess in the fatty tissues and fatty compounds it renders these tissues and compounds unstable.

Nothing outside of our observation has been found upon which to base a conclusion as to just what period of time is required for this transition, but evidently this period is measured by years. Certain tissues undoubtedly retain their constituents longer than others. For example, it is reasonable to suppose that the residence of fat in adipose tissue is of longer duration than fat in the skin. Certain individuals may use up their fatty tissue and replace it more rapidly than others. The state of an individual's health also plays a part in the destructive and constructive metamorphosis of this tissue.

It appears that it is necessary for oil to be consumed for not less than a year and when the time has been so short there is always a history of excessive use. These patients have used the fat exclusively and in many cases have seasoned boiled vegetables with it and have eaten much of fried foods. Almost invariably the pellagrin admits that he eats more greasy food than any other member of the family. This is especially true when the pellagrin and the other members of his family have previously enjoyed equal health.

In getting the history of oil consumption, the past eighteen months should be covered. Much difficulty is occasionally experienced, owing to the ignorance of some as to what they are eating. An intelligent patient states that he raises his own hogs and renders his own lard; denies visiting anywhere for any length of time. His

FIGURE IV.—JUNE, 1912.

wife supports these statements, yet it is finally shown that he has bought hogless lard for eighteen months prior to his first attack. An intelligent grocer states that he sends the lard from his own store, and never uses anything but pure lard. Upon request, he exhibits six empty buckets, only one of which is labelled "lard."

One significant point that may be mentioned here is that except in children under one year of age, all pellagrins, about four hundred in number, that I have had the opportunity of making an investigation, have been cottonseed oil consumers. It is hard to believe that this association of oil consumption with pellagra is accidental.

We have recognized the fact that many people have consumed cottonseed oil in some of the various forms for years without apparent injury, and this has led to inquiry among our patients not suffering with pellagra as to how many were eating cottonseed oil and how long they were using it. The results were as follows:

Forty-eight per cent. were users of cottonseed oil products.

Eighty per cent. of these date the beginning of its use within the past three years.

Many of these patients showed symptoms of pellagra.

When we admit that the fat of the body has long residence therein, requiring months for any given area of fat to be utilized and replaced from the food which enters the body; that adipose tissue may remain intact for months, or even years, it becomes clear that the pellagrin will be liable to attacks just so long as his adipose tissue contains linolin. Also, that by reduction of adipose tissue he will become immune to attacks until the linolin is reintroduced into his body.

Thus the period of accumulation or eradication becomes very variable according to the diet, health and individual disposition towards fat. We find such variation among our cases.

There is reason to believe that if linolin does not exceed a limited per cent. in a mixture of fats it will, on account of the ease with which it undergoes oxidation, be utilized before the more stable fat, thus being removed from the body and not accumulating in harmful amounts.

Just here it is interesting to note the physiological law which governs the deposit of fats. This law and this theory explain why the dermatitis is always more severe on the extremities and face when all parts are equally exposed to sunlight. Physiological compensa-

tion probably operates to reabsorb and transport the more liquid fats to the extremities, thus explaining the recurrence of dermatitis in these parts as long as three to twelve months after a previous attack, even though linolin has been excluded from the diet.

We were able to fix the number of years of oil consumption in seventy-three of our cases, as follows:

4 had eaten cottonseed products 1 year before first attack.
10 had eaten cottonseed products 2 years before first attack.
16 had eaten cottonseed products 3 years before first attack.
12 had eaten cottonseed products 4 years before first attack.
10 had eaten cottonseed products 5 years before first attack.
10 had eaten cottonseed products 6 years before first attack.
2 had eaten cottonseed products 7 years before first attack.
6 had eaten cottonseed products 8 years before first attack.
2 had eaten cottonseed products 9 years before first attack.
1 had eaten cottonseed products 10 years before first attack.

In Group VII we have twenty-four cases who used cottonseed oil continuously, or until a few months of the succeeding hot season. The cases who continued to eat oil products up to the time of the attack, or through the previous fall, had an equally severe recurrence. Cases Nos. 63, 80, 89, 91 and 94 represent a class of cases that have never had a severe attack. These mild cases always give a history of either interrupted oil consumption, very little oil consumption, consumption of oil in the fall of the year only, or oil consumption for a short period of time. A case not included in the table gave a history of eating compound lard in the fall of the year for twenty-two years, and of recurrent attacks of pellagra eighteen years.

Cases Nos. 94, 83 and 56, consuming oil in this manner, had mild attacks annually for twelve, eight and four years respectively, without any serious impression of the malady.

Name	Sex	Oral	Gastro-Intest.	Genital	Dermal	Nephritic	Mental	Result
M. W.	F	X	X	X	X	Slight	X	Death
L.	F	X	X	X	X	XX	X	Improved Still in Asylum
E. H.	F	X	X	X	X	XX	X	Death
F. J.	M	X	X	O	O	X	O	Improved
A. G.	M	X	X	O	X	X	O	Well
J. W.	M	X	X	O	O	X	O	Well
L. A.	M	X	X	O	X	X	O	Well
E. D.	F	X	X	O	X	X	O	Well
E. V.	F	X	O	X	X	X	X	Death
L. A.	M	X	O	O	X	X	O	Well
D. J.	M	X	O	O	X	O	X	Death
C. S.	F	X	O	O	X	O	O	Well
M. M.	F	X	X	X	X	O	O	Well
J. W. O.	F	X	X	X	X	X	X	Death
L. D.	M	X	X	O	O	X	X	Death
V. C.	F	X	X	X	X	X	O	Death
S. O.	F	X	X	X	X	X	X	Death
G. P.	F	X	X	X	O	X	O	Well
M. D.	F	X	X	X	O	X	O	Well
J. G.	M	X	O	O	X	O	O	Well
H. W.	F	X	O	X	X	X	O	Well
I. H.	F	X	X	X	X	X	X	Well
H. W. B.	F	X	X	X	X	X	O	Well
M. M.	F	X	X	X	X	O	O	Well
W. J. M.	M	X	X	O	X	X	O	Well
H. M.	M	X	X	O	X	XX	X	Death
E. W.	F	X	O	X	X	X	O	Well
A. H.	F	X	X	X	X	X	O	Well
J. B.	M	X	X	O	X	X	X	Improved
D. H.	M	X	X	O	X	X	O	Well

In the table we find sixty-two people who discontinued the use of oil and had no attacks in 1912. Two, Nos. 22 and 60, had no attacks in 1911. All of these people discontinued the use of oil in August or earlier except Nos. 1, 2 and 33. These three were on

a diet in the summer and fall of 1911 which excluded this food product and during the winter ate very little greasy food.

The cases of Group VIII, it is to be noted, had discarded oil several months but had a recurrence in 1912, though with one exception these patients were in much improved or good health. They had no symptoms except a slight dermatitis. The one exception, No. 67, continued the use of oil through November, 1911, and suffered a severe attack in April, 1912; he has made a good recovery, and in September was in good health.

We have already mentioned the possibility of the long residence of fat in the body and that as the more liquid fat of the extremities and face are oxidized they may be replaced by the more liquid fat which had been deposited near the warmer parts of the body.

So we would expect those cases who had suspended consumption of this class of fats to have an attack of dermatitis even after several months if exposed to the exciting causes. Illustrating this point is case No. 71. This patient suspended oil consumption in October, 1911, and on December 16, 1911, she had her first attack. The dermatitis affected the area which shows normal in Fig. 1. On January 11, 1912, she had another attack, which affected the area shown in Figs. 1 and 2. In June, 1912, a third attack, as shown in Fig. 3, on right hand. Figs. 3 and 4 show a pigmentation of the area affected in January. In July, 1912, she had the dermatitis on the left hand. The winter attacks were severe, while the summer attacks were representd by a slight dermatitis with no constitutional symptoms.

The cases of Group VIII had not eaten cottonseed oil products for the following number of months before the last attack.

Case No. 66, no cottonseed oil in 7 months.
Case No. 67, no cottonseed oil in 5 months.
Case No. 68, no cottonseed oil in 9 months.
Case No. 69, no cottonseed oil in 9 months.
Case No. 70, no cottonseed oil in 9 months.
Case No. 71, no cottonseed oil in 8 months.
Case No. 72, no cottonseed oil in 8 months.
Case No. 73, no cottonseed oil in 7 months.
Case No. 74, no cottonseed oil in 7 months.
Case No. 96, no cottonseed oil in 9 months.

Case No. 97, no cottonseed oil in 9 months.
Case No. 98, no cottonseed oil in 10 months.
Case No. 99, no cottonseed oil in 11 months.

If time permitted, we could show that the severity of the last attack and the state of health of the pellagrin is in proportion to the length of the period that oil had been discarded and the extent of emaciation present when it was discarded.

Age.—All ages appear among these cases. Case No. 100 is a child, eight months old, born in Atlanta, and had not been out of the city. His father was a pellagrin and his mother showed some symptoms, but was in fair health. The child, of course, does not eat cottonseed oil products, but we only need to mention that the infant comes into the world with a store of fat and an excess of lecithin which is probably not used up in the first months of extrauterine life, and that the fatty tissues of its body comes from and is influenced by the food of the mother.

Of the one hundred cases, thirteen are under twenty years of age; sixty are between twenty and forty years; and twenty-seven are over forty.

Sex.—Seventy-nine out of the one hundred are females. It is interesting to note that at the extreme of life this preponderance of females is not so marked. Of nine under fifteen years of age, five are girls, while of those over fifty years of age, nine are women and five are men. The preponderance of gastrointestinal disorders among women in this section, together with disturbances incident to sexual life, may account for the difference in incidence in the sexes. Sixty-three per cent. of gastrointestinal cases coming for treatment are women. It cannot be doubted that chronic diseases, such as some female disorders, predispose to pellagra. It is a notable fact that pellagra in the otherwise healthy is comparatively rare.

Residence.—In designating the residence, no cases are classified as urban unless they have lived in the city for two years when the first attack of dermatitis appeared. Those living in towns of less than three thousand inhabitants are classified as rural.

The table shows sixty-two cases of urban residence and thirty-eight cases of rural residence. These cases have made no material change in residence during the years of observation.

The incidence of pellagra among farmers is entirely limited to those who are using cottonseed oil. Much more corn products are consumed per individual by rural inhabitants and the western product is as much in use among them as among urban inhabitants.

Seasonal Incidence.—The one hundred cases have had 170 attacks of dermatitis, the months of which could be ascertained. The month of incidence is as follows:

January	2	July	31
February	2	August	8
March	17	September	4
April	24	October	2
May	39	November	0
June	40	December	1

Attacks occurring in the winter are not rare and we must admit other exciting causes than seasonal influences.

CLINICAL AND PATHOLOGICAL NOTES ON PELLAGRA.[1]

By C. W. G. ROHRER, M. D., Maryland State Department of Health, Baltimore, Maryland.

INTRODUCTION.

The clinical symptoms of pellagra, as observed in the Maryland cases, are numerous and varied. The best I can do is to attempt to classify them in such a manner as to aid in future recognition of the disease, and in its ultimate suppression. While pellagra is not a reportable disease in Maryland, its distressing symptoms and almost uniform fatality have rendered it a terror to the citizens of certain sections of the State. For this reason I believe every case has been brought to the notice of the proper health officials.

In regard to the pathology of the disease, I must admit that but few autopsies have been performed upon pellagrins in Maryland. The discordant results in such as have been performed make a pathological report unsatisfactory and well nigh impossible. However, I have incorporated in the present paper a summary of these findings, which I shall now submit to this body for whatever they may be worth.

NUMBER OF PELLAGRINS.

As mentioned in my paper of yesterday, entitled, "Pellagra in Maryland," thirty-one cases of the disease have occurred in Maryland down to the present time. Nine who acquired the disease resided within the corporate limits of Baltimore, the metropolis of the State, and twenty-two who acquired it resided in the smaller cities, towns or rural communities.

Several of the Maryland pellagrins were children, but a majority of them were adults who had passed the meridian of life. White persons and colored persons, males and females, old and young, are affected indiscriminately.

There is only one feature that is constant, regarding the Maryland cases of pellagra. It is this: All thirty-one cases of pellagra in Maryland have occurred in the two geographical divisions of the

[1]Paper read at the second triennial meeting of the National Association for the Study of Pellagra, held at Columbia, South Carolina, October 3 and 4, 1912.

State known as the Coastal Plain and the Piedmont Plateau. Thirty of the cases originated in the former region and only one in the latter.

COLOR AND SEX.

The color and sex of the 31 Maryland pellagrins may be stated briefly, as follows:

Table No. 1.—Color and Sex of Maryland Pellagrins.

	White.	Colored.	Male.	Female.
Number of Cases.....	25	6	15	16

In regard to color, it can readily be seen that white patients largely predominate, there being four times as many white pellagrins in Maryland as colored ones. However, when the percentage of white pellagrins in proportion to the total white population is calculated, and the percentage of colored pellagrins in reference to the total colored population is determined, the disparity is not so striking. For example: The total population of the State of Maryland, Census of 1910, is 1,295,346, of which number 1,062,644 are white persons, 232,249 colored persons, 376 Chinese, 22 Japanese, and 55 Indians. As yet, no cases of pellagra have occurred in any of the latter three nationalities. Hence, we can exclude these persons, and on getting down to figures we find the proportion of pellagrins among the white population of Maryland is 2.35 per 100,000, while among the colored population the proportion is only slightly higher, namely, 2.58 per 100,000.

AGE OF MARYLAND PELLAGRINS.

These patients present a variety of ages, ranging from 6 to 77 years. A majority, however, were in the prime of life. The appended table (Table No. 2) will set this matter forth, in a clearer light.

Table No. 2.—Age of Maryland Pellagrins.

	1 to 5 Years.	5 to 10 Years.	10 to 15 Years.	15 to 20 Years.	20 to 25 Years.	25 to 30 Years.	30 to 35 Years.	35 to 40 Years.	40 to 45 Years.	45 to 50 Years.	50 to 55 Years.	55 to 60 Years.	60 to 65 Years.	65 to 70 Years.	70 to 75 Years.	75 to 80 Years.	80 Years and Over.	Total.
Number of cases.....	...	2	2	1	...	1	2	3	3	3	3	2	6	1	1	1	...	31

According to the above table, the most susceptible age-period in Maryland is from the 60th to the 65th year. The next most susceptible period ranges from the 35th to the 55th year. In fact, 20 of the 31 Maryland cases occurred between the ages of 35 and 65 years. Only five of the patients were under age.

DURATION OF ILLNESS.

Pellagra may be acute or chronic, a majority of the Maryland cases being of the latter type. In some of the Maryland cases the duration of illness is given as "indefinite," while in others no information at all is available on this topic. The briefest period stated is six weeks; the longest, three years. The subjoined summary will elucidate this part of our subject.

Table No. 3.—Duration of Illness.

	6 Weeks.	8 Weeks.	3 Months.	4 Months.	5 Months.	8 Months.	10 Months.	1 Year.	1½ Years.	2 Years.	3 Years.	Unknown.	Total.
Number of cases.....	1	1	1	2	2	1	1	1	1	6	1	13	31

Judging from the above figures pellagra is generally a chronic disease in Maryland, a period of two years being its average duration. In such cases the disease ordinarily abates during the summer season, to flare up again in the spring or fall, usually in the spring.

CLINICAL HISTORY.

It would be impossible for me, in the space of time at my disposal, to give complete clinical histories of all the Maryland cases of pellagra. I shall, therefore, give a summary of several of them which appear most typical of the disease.

CASE 3, MARYLAND SERIES.

Patient is a white female, unmarried, aged 52 years, a lifelong resident of Charles county, Maryland. She did housework and also assisted with the work on the farm. She has four sisters and six brothers, all living. Her mother is also living and in good health, at the age of 78 years. Her father died of typhoid fever when he was 60 years old. One sister has muscular tremor, which resulted, so she stated, from an attack of Hodgkin's disease seven years previously. All of the members of the family go barefooted in the summer season.

Patient had the usual diseases of childhood, but no serious illness prior to the present trouble. This is her third attack, having had her first attack two years ago and her second one a year ago, beginning in April in each instance. Gastric disturbances harassed the patient for three or four years before the skin lesions appeared. She drank hot water for her "dyspepsia," and became much reduced in weight by a troublesome diarrhœa. Then the skin lesions, spots of erythema characterized by a fiery redness, appeared, first on the wrists, then on the forehead, and a few days later on the dorsal surfaces of the feet. Her appetite was poor, and she seemed to relish nothing but ice cream. Her temperature ranged from 99° to 100° F., up until the last week of her life, when it became subnormal. The usual ratio between pulse and temperature was maintained, the pulse becoming less frequent when the temperature became subnormal. She had severe, ulcerative stomatitis. Her mental condition, which was bad when she entered the hospital, grew progressively worse.

CASE 7, MARYLAND SERIES.

Patient is a white male, a carpenter by occupation, addicted to the use of alcoholic liquors all his life. He had the usual diseases of childhood, including scarlet fever, and at the close of the Civil

War he was a sufferer with chronic diarrhœa, from which he recovered. The present trouble began two years ago, and was ushered in with vague and indefinite gastric disturbances as follows: pain in stomach and griping, about an hour after the morning meal, followed by a watery stool, the whole train of symptoms consuming about 15 minutes of time. Occasionally there would be vomiting. There were no other symptoms until the skin lesions appeared, four weeks prior to the patient's death. These began with a tingling sensation on the back of the patient's right hand, followed by intense redness extending over an area the size of a half dollar. It appeared to the patient that blood was spreading under the skin as if a vein had burst. About five minutes later the process began in the other hand. There was no itching, and the fiery redness was followed by a number of small blebs or blisters. His tongue and tonsils became irritated on the same evening that the eruption appeared on the backs of his hands.

CASE 8, MARYLAND SERIES.

Patient is a white man, aged 37 years, married. He was born in Martinsburg, West Virginia, but has resided in Baltimore, Maryland, for the last fifteen years. A pipefitter by occupation. Patient had the usual diseases of childhood, including scarlet fever, as in Case 7, of the Maryland series. All his life he has used intoxicating beverages freely. The present attack is the only one the patient has had, and dates back about one year. Began with pain in stomach after eating, morning diarrhœa, and occasionally vomiting. For several weeks he has had pain on swallowing, and stomatitis has been a marked symptom only for about one week. The skin lesions first began on the feet, and later on the hands. From the onset of the first symptoms one year ago, patient has been losing weight and strength. His appetite has not been good, his sleep disturbed, and he is very apathetic.

NOTES ON PATHOLOGY.

The pathology of pellagra is still somewhat obscure, because comparatively few autopsies have been performed upon patients dying of this alleged new disease. It is to be sincerely regretted that such is the case, because clinical symptoms and autopsy findings should go hand in hand in the solution of the perplexing problem of pellagra.

Pathological anatomy is one of the handmaids to medicine, and the elucidating science of bacteriology is another. I believe that when more autopsies have been performed on persons dying of pellagra, and when more cultures have been taken during life and at autopsy, the keynote to the situation will be discovered. We shall probably find that pellagra is not a germ disease, that its pathology varies with the duration of illness and the number and nature of complicating disorders, and that its existence depends upon a perverted and predisposed constitution. We shall probably revert more nearly to our original opinion, namely: that pellagra is a cachectic condition occurring in predisposed persons; that it has for its basis some chronic nutritional or assimilative disturbance; and that diet, personal hygiene, and the aid of a few drugs will, in a majority of instances, restore the patient to health and strength.

I shall first append a few notes on the pathology of pellagra, written April 28, 1910. These are as follows:

"The pathology of pellagra is not constant. Different observers have described different pathological changes. These are usually discussed under the following three headings:

"1st. The changes in the intestinal tract.

"2d. Changes in the nervous system.

"3d. The changes in the skin.

"The changes in the intestinal tract consist of atrophy of the muscular coat, with intense hyperemia and occasionally ulceration.

"The most constant post-mortem lesion is alleged to be in the lateral columns of the spinal cord. This condition is one of degeneration, and it is most pronounced in the dorsal region. Practically no changes are seen in the lumbar cord.

"The skin changes are erythematous in type. At first there is congestion, followed later by pigmentation, and finally by desquamation.

"Of the four cases of pellagra occurring at the Mercy Hospital, which have just been described by Dr. Lockwood and Dr. Beck, two came to the autopsy table. They were Cases 3 and 6[1] of the series of seven cases of pellagra which have occurred in Maryland.

"Our first pellagra autopsy was performed on a chronic, recurrent case of the disease in August of last year (1909). A striking feature was the presence of numerous granuloma-like bodies.

[1]Case 7, of the revised list appearing in the present paper.

When examined by the microscope these small tumor-like nodules or granulomata ('pseudotubercles') are seen to be composed of a necrotic center surrounded by spindle-shaped cells and small round cells.

"These granulomata are most abundant in the walls of the superficial blood vessels of the lungs, especially those of the upper lobe of the right lung. Next to the lungs rank the superficial blood vessels of the brain. Granulomata are also found in the stomach, intestines, spleen, kidneys and uterus.

"Another feature is the intense congestion noticeable in practically all the tissues and organs. An extreme degree of gastroptosis and enteroptosis was also pointed out at the autopsy.

"The liver showed chronic passive congestion, with numerous bacterial emboli in its smaller vessels.

"The stomach at its lower fourth is encircled by many varicose veins. Attached to several of these veins is a polypoid growth.

"The kidneys contain several small cysts, and show a condition of chronic diffuse nephritis. Numerous necrotic areas are also seen. The cortex is narrow, measuring but one-eighth of an inch.

"The heart weighed but five and one-half ounces, and its interior was filled with white clot. The proportion of the weight of the heart to the weight of the body was as 1 to 233, the patient having been reduced to 80 pounds in weight. The heart also showed the condition known as 'drop-heart.'

"With the exception of slight degeneration of the lateral columns of the cervical portion, the spinal cord shows no conspicuous change.

"The blood vessels of the brain contain numerous granuloma-like masses. The brain weighed nearly forty-four ounces.

"The skin shows degeneration of its epidermic layers. The deeper of these have been transformed into keratin; the superficial layers have become gangrenous. The *cutis vera*, or true skin, shows little or no involvement.

"At our second pellagra autopsy performed on the 17th of the present month (April, 1910), but few granulomatous masses ('pseudotubercles') were found. These were confined to the lungs.

"There was, in this second autopsy, intense erythema or congestion of the entire alimentary tract. The rectum showed lesions which were probably healed ulcers.

"The mesenteric lymph-glands were markedly enlarged. This was one of the most interesting features noted at this autopsy.

"The brain showed edema, with congestion of its anterior portions.

"The skin lesions, confined chiefly to the hands and wrists, consisted in erythema, pigmentation and desquamation of the cuticle.

"To the naked eye the remaining tissues and organs appeared normal, excepting the thyroid body, which was atrophied.

"Microscopical sections from this second pellagra autopsy have not been studied.

"The subject of pellagra is of growing importance, and it is hoped that these few scattered remarks will stimulate an increased interest in the matter.

"Maryland physicians having suspected cases of pellagra should seek the co-operation of the city or State Department of Health."

Apropos of the foregoing paragraphs I wish to make a few amplifying remarks and add a few additional notes on the microscopy of pellagra. Upon further study I have found that many of the granuloma-like masses or "pseudotubercles" described above are in reality vascular thrombi in various stages of organization. These have formed in the superficial vessels and also in the terminal vessels, causing, as in the case of the kidney, areas of focal necrosis.

This thrombosis of the superficial and terminal vessels is of especial interest as appertaining to the skin and mucous membranes. It constitutes, as I believe, the essential lesion in the production of the primary erythema and the secondary gangrene. Microscopical sections of the skin and of the rectum show this condition beautifully. In both instances where the superficial vessels are occluded, gangrene and sloughing have resulted.

To summarize: The following are the essential pathological lesions detected at autopsy on the Maryland pellagrins:

1. Thrombosis of its superficial blood vessels—cutaneous, mucous, and parenchymatous, pathological entities which I believe are responsible for the initial hyperemia and moisture of the skin and its subsequent gangrene and denudation; for the erythema, gangrene and ulceration of the intestinal mucosa; and for the infarcts found in the kidneys, spleen, etc. It might be of interest to add that many of the lesions which I described in a previous paper as "granulo-

mata," have been found to be thrombi in various stages of organization.

2. A marked degree of ptosis or displacement of all the abdominal viscera.

3. Sclerosis of the blood vessels and of the parenchymatous organs—liver, spleen, pancreas, kidneys, etc. Even the pituitary body was markedly involved.

4. Enlargement of the mesenteric lymph-glands.

5. Atrophy of the thyroid body.

6. Evidences of chronic gastritis.

HISTORY OF RECOVERED CASE.

The one recovered case of pellagra in the Maryland series of 31 cases has awakened unusual interest, and I shall append herewith entire a letter descriptive of it, received from Dr. Louis B. Henkel, Jr., one of the best known physicians of Annapolis, Anne Arundel county, who attended the patient.

ANNAPOLIS, MARYLAND, September 30, 1912.

Dr. C. W. G. Rohrer, State Board of Health, Baltimore, Maryland.

DEAR DR. ROHRER: In accordance with your request I beg to give you all the information that I can at this time obtain, in reference to the case of "pellagra" which I attended about one year ago, to wit:

Ephraim Ennis, colored, aged 10 years, son of J. W. Ennis, colored, living at Davidsonville, Anne Arundel county, Maryland. The case was referred to me at the Emergency Hospital, Annapolis, by Dr. Albert G. Webster, with a history of having had an attack of supposed enterocolitis followed by emaciation, staggering gait, and scaly eruption of the hands and feet, which symptoms were more or less of a chronic nature. The earliest symptom appeared on or about May 15, 1911, and I first saw him on July 12, 1911.

At the time I was at a loss to know exactly what might ail the boy. However, I studied his case rather thoroughly, and during his stay in the hospital I had numerous physicians to see him in consultation, among whom were Dr. Joseph C. Bloodgood, of Baltimore; Dr. George Pickrell, U. S. N., and the entire medical staff of the Emergency Hospital. They all agreed with me that the case was very suggestive of pellagra; but only Dr. Pickrell and Dr. Bloodgood had seen cases, and their opinion coincided with mine.

I was only able to get an incomplete history from the boy's parents, and that was an obstacle in reaching a diagnosis. I have just heard from a resident of Davidsonville, and he informs me that the boy is working and in excellent health so far as he can judge.

The treatment which I gave the boy, and which was continued after he left the hospital on August 13, 1911, was, after a few days of preliminary purging, etc., house diet, Fowler's solution of arsenic, hexamethylenamin and santonin, the latter drug being given him after he had vomited a round worm. I might say that I kept the boy in the open air as much as possible, and also gave him a ferruginous tonic after he left the hospital.

Dr. Rohrer, I am sorry that I cannot at this time give you a more definite description, but if you so desire, I am willing to get it up for you at some future date. The charts at the hospital have been mislaid, and I am therefore giving you what information I can recall from memory.

Hoping this will give you some idea of this case, and assuring you that I am always ready to give you further information, I remain, Yours very truly,

(Signed) LOUIS B. HENKEL, JR.

I need hardly state that the foregoing description is one of the most lucid which we have concerning a case of pellagra from the inception of the disease until complete recovery of the patient. A careful perusal of it will aid the merest tyro in diagnosing the disease, while the line of treatment followed holds out suggestive hints on therapy.

CONCLUDING REMARKS.

In conclusion I desire to state that a careful study of the clinical history and pathology of pellagra has convinced me that there are two or three requirements to be met, in order to treat this disease successfully.

1. In regard to diet. A strict regimen should be followed, as indicated in Dr. Henkel's letter quoted above.

2. Tonics should be given to overcome the alarming cachexia.

3. Hypodermoclysis, using normal salt solution, to increase the amount and fluidity of the blood, is undoubtedly of service. This would diminish the tendency to thrombosis in the superficial vessels,

and also aid in the absorption of thrombi already formed. In many cases the profuse, watery diarrhœa attendant upon them makes hypodermoclysis almost imperative.

4. In chronic, recurrent cases of pellagra alteratives are of service, to counteract the symptoms due to sclerosis of the blood-vascular system and the parenchymatous organs. Cases apparently cured or relieved by the administration of salvarsan, Ehrlich's specific for syphilis, are probably those in which such changes are paramount.

A CASE OF BERI-BERI PRESENTING AN INITIAL ERYTHEMA RESEMBLING PELLAGRA.

By ROBERT WILSON, JR., M. D., Charleston, S. C.

The following case came under my observation in the summer of 1910:

The patient was a medical student twenty-two years of age and a native of Virginia, who had been living at Charleston since October, 1909. His family history was good, his father having died at the age of fifty-three of "acute indigestion," and his mother being still alive and in good health. He had two sisters, both of whom were in good health; two brothers who had died of diphtheria.

His personal history included measles, whooping cough, mumps and scarlatina, all of which he had had in childhood, and grip, which he had had twice, the last attack being two years prior to his present illness. His habits were good and no venereal history could be obtained. In May, 1910, he accepted a position in a drug store on Sullivan's Island, a seashore resort lying at the mouth of Charleston harbor.

His illness began four weeks before his visit to me, August 29th, with œdema of the lower extremities, pitting on pressure, slight in the morning and rather well marked in the evening. He was also troubled with slight dyspnœa upon exertion. About two weeks before consulting me a sharply defined erythema had appeared upon the back of each hand, extending from the base of the phalanges to the wrist. He also suffered somewhat from muscular weakness, headache, and backache. When I saw him for the first time the erythema was well marked and closely resembled sunburn. His tongue was red; appetite and digestion fair; bowels active; heart apex in fifth interspace, with no displacement to the left, but a clear systolic murmur was heard in both the mitral and aortic areas; pulse normal; hemogloben 85%. A differential count was not made, neither did I look for plasmodia malariæ, there being no suggestion of malarial symptoms. The knee jerks were present, but sluggish; the urine showed a specific gravity of 10:10, but was otherwise normal.

The erythema began to subside and a branny desquamation to appear about the first week in September and had disappeared about

the twelfth, when he consulted me about the advisability of returning to his home in Virginia. He also complained at this time of extreme weakness. The heart murmur was still present, but the œdema had partially subsided.

He reached Leesburg, his home, in such an exhausted condition that he had to be carried to his house where his physician, Dr. John A. Gibson, saw him immediately. Dr. Gibson wrote me that his examination showed "pupils dilated; skin moist; ocular reflexes impaired; inability to use either hands or feet; temperature 100; pulse 160; heart action weak, with well defined mitral murmur. Blood examination showed malarial plasmodia in abundance; lymphacytes both large and small; urine dark and scanty, only six ounces voided in first twenty-four hours by catheterization; stool very dark and foul, bile pigment present, otherwise normal."

Improvement began very shortly and in three weeks he could be carried to Dr. Gibson's office for electrical treatment. A week or two later he was able to stand, from which time improvement was progressive until the end of December, when he had recovered entirely and returned to Charleston. When I examined him at this time he was perfectly well and the cardiac murmur had disappeared.

The diagnosis of beri-beri, which was made independently by myself and Dr. Gibson, and concurred in by Dr. Irving J. Spear, of Baltimore, was based upon the association of cardiac disturbances and œdema of the lower extremities with the symptoms of a mixed form of multiple neuritis, other ordinary causes of such a condition being excluded.

The most interesting features in this case were:

First, its sporadic occurrence. While cases of beri-beri have been reported in Charleston during the last few years among the inmates of the jail, and among the convicts in a camp located about ten miles from the city, no other case had occurred upon Sullivan's Island.

Second, its development in a young man moving in the upper walks of life and whose surroundings for the previous ten months had been most excellent.

Third, the appearance of an initial erythema resembling pellagra. Manson[1] speaks of the absence of erythema in beri-beri as being one of its distinguishing features. On the contrary, A. A. De Azevedo Sodre,[2] of Rio de Janiero, writing on beri-beri in the Twen-

tieth Century Practice of Medicine, says that "some patients suffer from cutaneous eruptions of various forms, similar to those of roseola or erythema." I was able to obtain from the Surgeon General's office in Washington only one report of beri-beri associated with an erythematous eruption. This case was reported by Dr. T. K. Monroe,[3] of Glasgow, Scotland, in the London Lancet, under the title of "A Case of Ship Beri-Beri, Associated With an Erythematous Eruption." Monroe's patient was a Scandinavian fisherman, who had been in good health until August, 1907, when his hands became red and swollen; three days later the legs began to swell and the calves became painful. In five days after the commencement of the attack the face became red and swollen. On admission to the Glasgow Royal Infirmary, eight days after the onset of the attack, there was redness of the face and neck, with irregular patches of erythema on the upper arm, shoulders and back and over the pectoral muscles. There was a diffuse erythema, disappearing on pressure, over the entire lower limbs for almost the whole length. The erythema disappeared eight days after admission. The diagnosis of beri-beri in this case was based upon a subsequent development of cardiac disturbances and the characteristic polyneuritis.

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THE COEXISTENCE OF PELLAGRA AND BERI-BERI.

By ELEANORA B. SAUNDERS, M. D., Assistant Physician, State Hospital, Columbia, S. C.

Among the clinical problems of American medicine, none at present is of more absorbing interest than the study of the protean forms of pellagra. Both diagnosis and prognosis are difficult and uncertain because of the polymorphous character and the unexpected episodes of the disease. In new cases, developing from year to year, different phases are emphasized. Old cases also display this variability with every recrudescence. In one season the skin lesions are marked; in another the intestinal symptoms are pronounced or again nervous phenomena predominate. In other words, the disease is inconstant in its evolution in time, in place and in person. Hence in part, at least, our difficulty of orientation regarding it. While this variability is true of other diseases, its relationship to pellagra is notably striking.

During the current year many of my patients have shown severe nervous symptoms, both central and peripheral. Since the first recognition of pellagra in our hospital in 1907 the development of tabetic and other spinal complications has been observed from time to time, but prior to 1912 there has been no recognition of pellagra with symptoms of multiple neuritis. Neuralgic pains and paresthesias, it is true, have not been uncommon. This year, however, some of my patients have had in addition to peripheral nerve involvement, distressing symptoms due to cardiac conditions and edema. I have, therefore, considered the syndrome as suggestive of beri-beri and this disease could not be excluded differentially.

We may recall that reports of the occurrence of beri-beri in asylums, though rare, are not new, as is noted by Braddon.[1] Bondurant[2] reported a series of 71 cases with a mortality of 21, from the Bryce Insane Hospital at Tuscaloosa, Ala., during the years 1895 and 1896. Barner[3] reported the disease from the Little Rock, Ark., Asylum in 1898. In 1907 over 200 cases of beri-beri developed in the State Lunatic Asylum at Austin, Texas.[4] Of these 20 were fatal.

Abroad beri-beri was observed by Norman[5] at Richmond Asylum, near Dublin, Ireland. Norman also regards as suspicious of beri-beri, epidemics which occurred among asylum patients at Saint Gemmes-Sur-Loire, France, and at the Suffolk County Asylum at Melton, England (Braddon).[6] Some short though convincing notes upon the relation of polished rice to beri-beri among his asylum patients were published in 1911 by Gibbs,[7] Medical Superintendent of the Singapore Lunatic Asylum. This wide geographical distribution of beri-beri and its occurrence among the insane deserves more than passing comment. No less authority than Sir Patrick Manson[8] has pertinently suggested that many of the forms of multiple peripheral neuritis seen in temperate climates are really sporadic cases of beri-beri. This suggestion, together with the above citations, may well serve to put asylum medical officers on the alert when cases of neuritis appear among their patients.

Previous reports of beri-beri in South Carolina have also been made. In 1910 an epidemic of this disease, first discovered by Jervey[9] in a convict camp near Charleston, aroused much interest. These patients, having been removed to the State Penitentiary in Columbia, were studied and reported by Long[10] and by Butler.[11] About the same time a few cases of beri-beri were observed also at our State Hospital. Furthermore, Dr. Robert Wilson, Jr.,[12] has reported from Charleston a case of multiple neuritis, probably beri-beri associated with a pellagroid erythema. No doubt can therefore be entertained of the previous existence of beri-beri in South Carolina.

As an anti-pellagra experiment, in August, 1911, by order of the Board of Regents and the Superintendent, all corn products were excluded from the dietary of our hospital, and since then rice has been used more plentifully. Following the increase in the ration of rice, cases of peripheral polyneuritis as well as neuritis associated with other diseases, especially pellagra, have become more frequent. Samples of this rice were submitted to Dr. C. L. Alsberg, Chemical Biologist of the Department of Agriculture, Washington, who reported that "It contains 0.14 per cent. P_2O_5 or 0.06 per cent. phosphorus. The amount of phosphorus is therefore very small. In fact, it seems to be slightly less than has been reported by Aaron for polished rice in the Philippines."

The following is a brief case-history of uncomplicated, but recurring beri-beri in one of my white insane patients:

Mrs. M., admitted in 1900. Aged about 40 years. Mother of six children. She gradually became demented, though her bodily health continued good. In the spring of 1910—that is, at the time of the first observation of beri-beri among our patients as noted above—having previously been noisy and restless, she became languid, less inclined to exertion, and lost appetite. She soon began to complain of pain in feet and hands. The symptoms of peripheral neuritis were then first noticed. The pain became agonizing, her feet and hands being so sensitive that she screamed at the slightest touch. Even the pressure of the bedding was painful. This symptom is noted by Scheube,[13] who also speaks of "spontaneous pains." Because of the pain and subsequent paralysis Mrs. M. became helpless. Over the tibiæ edema was marked, nor was it to be confounded with the glossy, swollen appearance of the hands and feet in simple neuritis. Ascites also developed. There were marked circulatory disturbances. On inspection throbbing vessels of the neck were noticed, also a diffuse impulse over the cardiac area as well as epigastric pulsation. The area of cardiac dullness was increased and a distinct systolic bruit was audible at the base. The pulse rate was quickened and the regularity of the heart's action was frequently disturbed. After months of illness, there was a slow return to normal bodily health. In May, 1911, the neuritis, edema, and heart disturbances reappeared. With rest in bed, careful dieting, etc., she gradually regained her previous physical condition. In May, 1912, there was a recurrence of the same clinical picture of polyneuritis, but of a milder type. After a few weeks she was able to walk with a fair degree of comfort and is now in good physical condition. No symptoms of pellagra have ever been observed in this patient.

To summarize: We have here the history of a woman, an asylum resident for 10 years, who in 1910 develops the classical symptoms of beri-beri, yet without the usual predisposing causes, such as fatigue, privation, or ill health. Polished rice, however, was an article of diet. Braddon[14] quotes Bondurant as having noted in the outbreak of beri-beri in the asylum at Tuscaloosa, Ala., that it was not the physically, but the mentally enfeebled, who fell victims to this disease.

Here the question forces itself upon us: Does the existence of insanity predispose lunatics to beri-beri as it undoubtedly does to pellagra?

In my cases, when the polyneuritic symptoms first developed, kidney and heart diseases being excluded, I suspected poisoning. The symptoms suggested alcoholic, arsenical or malarial neuritis, but as neither arsenic nor alcohol had been administered and as the plasmodium of malaria was at no time present in the blood, the diagnosis of beri-beri was made, being based upon the presence of lassitude, polyneuritis, edema and heart symptoms, including irregular pulse, palpitation and murmurs at the base, and finally emaciation. Hemic murmurs were excluded as the systematic examination of the blood during the course of the illness showed only a slight anemia. The subsequent annual recrudescences were probably due to reintoxication. Upon this point, Castellani and Chalmers,[15] referring to beri-beri, say:

"An attack does not confer immunity; on the contrary it rather predisposes to another attack. It is probable that there are no relapses but reinfections." (These authors, by the way, favor the parasitic etiology of beri-beri.)

In my wards, early in the spring of 1912, although the number of cases of pellagra had greatly lessened, some former pellagrins began to show the seasonal outbreak. Later, in addition to the usual pellagrous syndrome, symptoms of polyneuritis and distinct swelling over the tibiæ developed. One patient, though thoroughly demented, complained bitterly of pre-cordial distress and pain in hands and feet. Later she became paralyzed with wrist and foot drop. Cardiac irregularity and emaciation followed. These symptoms in a pellagrin naturally aroused suspicion of the possible association of beri-beri as a complication.

Whether there is a kinship between pellagra and beri-beri is still an open question. The symptoms of the two diseases, outlined below, seem to develop independently each of the other. The patients were all pellagrins with a history of vernal and autumnal exacerbations for several years prior to the appearance of neuritic manifestations. When the beri-beric symptoms appeared, the patients were already well advanced with pellagra. All were white women.

Miss McK., admitted October 3, 1907. A large, well nourished woman, for whom the mental diagnosis of constitutional inferiority was made. She was in fair health up to the spring of 1912, when she began to lose in weight, and complained of lassitude and indigestion. Later redness of tongue, brown hands and diarrhœa appeared. By rest in bed she improved, but while still confined to her room she complained of numbness of feet and hands, paresthesia and pain. The redness increased. Complete paralysis of hands and feet developed. Edema was manifested by pitting over the tibiæ, and by abdominal distention. Palpitation of heart followed. Again after a month's rest in bed she improved somewhat, but never regained the power of either co-ordination or locomotion. In June small areas over the knuckles became reddened, then this erythema spread over the hands, the skin of which became unusually thickened and discolored. The tongue and buccal mucosa became intensely congested and at some points blood oozed from the deep red membrane. Salivation appeared and this could not be overcome; the condition of her mouth and pharynx prohibited forced feeding. Her negativism became pronounced. Towards the end diarrhœa set in, producing great prostration. She died of exhaustion. Three weeks prior to death the blood findings of this patient were as follows: Red blood cells, 4,264,000, size and shape normal; white cells, 10,000; differential count: polynuclears, 70%; small lymphocytes, 22%; large lymphocytes, 4.8%; large mononuclears, 2.8%; basophiles, .4%. Malarial parasites were absent.

In all cases reported in this paper repeated examinations of urine, stools, and blood showed also practically normal conditions. Autopsy was not permitted in any case.

Miss McQ., aged 55 years. Family history negative. Pellagra developed in June, 1911. Her history stated that she was always thin, and of a nervous, restless temperament. When the mental symptoms became marked, she was transferred to the State Hospital (September 21, 1911.) Upon admission she was emaciated and anemic. Her hands were red and rough, her gait and station bad. She was confused, had hallucinations of hearing and was incoherent in speech. With rest, forced feeding and companionship, she improved in weight and the skin symptoms disappeared, but she remained untidy and resistive, and had little appetite. In March, 1912, her hands and tongue became very red. On account of weak-

ness she was kept in bed. At this time a slight apoplectic stroke, probably serous, occurred, from which she soon completely recovered. Then appeared signs of multiple neuritis, such as lack of co-ordination, pain, swelling of legs and abdomen, irregularity of the heart, cardiac murmurs and carotid and epigastric pulsations. Later wrist drop and meningeal symptoms followed. Lingering in this condition with alternating excitement and stupor, she died of exhaustion August 14, 1912.

Mrs. W., aged 53 years. Mother of six children. Was first admitted June, 1908, with a diagnosis of paranoid dementia precox. She was emaciated, refused food, and had ideas of grandeur. After some improvement she was taken home (July 7, 1908). In August, 1909, she was readmitted, her condition being worse both mentally and physically. There was a tendency to self-mutilation. Sitophobia was again dominant. In the spring of 1912, in addition to diarrhœa, stomatitis and dermatitis, there was a peculiar muscular flabbiness, especially in the calves of the legs. Cardiac symptoms and neuritis developed. Pain was so severe as to demand the use of large doses of opium. Complete paralysis of hands and feet followed, with edema over tibiæ, extensive trophic changes and emaciation. Her death on May 29, 1912, was preceded by meningeal symptoms, coma and rise of temperature to 106° F.

Mrs. S., aged 50 years. Was admitted in June, 1905, with diagnosis of dementia precox. She was cataleptic, at times noisy, untidy, delusional, but in fair physical condition. Six years later symptoms of pellagra developed. Early in 1912 the erythema, diarrhœa, and sore mouth reappeared. About March she became indolent and complained of precordial pain. This was soon followed by the symptoms of peripheral neuritis with ascites and edema of feet and legs. Other cardiac symptoms of beri-beri were noticed: dyspnea, irregular pulse and visible throbbing of the carotids. All mucous membranes became so congested that bloody serum oozed from mouth, nose, rectum and vagina. (Such a serohemorrhagic discharge is noted by Scheube[13] as a rare symptom of beri-beri and in his experience it ushers in death.) Strangely enough near the end the patient's mental condition cleared up sufficiently to enable her to describe her feelings and to lend co-operation in the efforts to relieve her. The illness was acute, death ensuing on the 26th day from onset.

The appearance of the symptoms of beri-beri in pellagrins is new in my service, or at least, the association has not been noted by me until this year. Similar cases, however, were observed at the same time in the three other departments of the hospital. Manson[16] says: "Multiple peripheral neuritis occurring as an epidemic or in a place in which the disease has occurred on previous occasions, may, as a rule, be set down as beri-beri." The patients whom I have described as developing beri-beri had all been asylum residents for at least a year and all had used rice freely. No form of arsenic had been administered to them.

CONCLUSIONS:

1. Pellagra and beri-beri may coexist.
2. In pellagra neuralgias and even polyneuritis may be present with no other symptoms indicative of beri-beri.
3. Symptoms of pellagra may be unmodified by the secondary development of beri-beri, or some cases of pellagra may be rapidly fatal in consequence of an acute complicating beri-beri.

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PELLAGRA IN CHILDREN, WITH OBSERVATIONS ON EIGHTY-FIVE CASES IN TWO ORPHANAGES.

By H. W. RICE, M. D., Columbia, S. C.

Although the prevalence of pellagra is now receiving extensive consideration by American physicians, I am not aware that the disease in children has been specially emphasized in this country. This paper, therefore, will deal chiefly with some observations upon two epidemics among children in orphanages, one occurring in a local institution where I have been the attending physician for the last six months, the other epidemic occurring in an orphanage in another part of the State, where I saw the cases with the physicians in charge of the patients.

When I became aware of the presence of these epidemics I made inquiry of other similar institutions as to their experience with pellagra. Of fourteen orphanages in this and other States that have been heard from, five have reported the existence of the disease among the inmates. In one orphanage twenty-four cases occurred last year, in another sixteen cases have occurred within the last few years with six deaths and ten recoveries. The other three institutions each report from one to five cases without deaths. So that it would appear that the disease as yet does not prevail extensively in such institutions. The fourteen orphanages care for about 3,000 children.

In the two orphanages where my observations have been made, there have been altogether seventy-one cases this year and there are fourteen other children who have had one or more attacks without recurrence this year. The children have been collected from various parts of this and other States, the pellagrins representing thirty different counties. Some of these children were suffering from the disease when admitted to the institution; and the impression prevails among the officers of both orphanages that the first cases were imported. This surmise, however, could not be verified as the history shows that pellagra existed in these institutions several years before it was diagnosed. The nurse at one of the orphanages, whose experience enables her to recognize the disease now, is confident that she found cases there when she entered upon her duties eleven years ago. This was six years prior to the recognition of

pellagra by Dr. Babcock in the South Carolina State Hospital in 1907. There are children in both orphanages who have had the disease for five years or more. In one of the orphanages there were twelve cases in 1907, twenty cases in 1910 and forty-three cases in 1912 with a less number in the intervening years.

Until this year the disease has been treated in one of these institutions as hookworm disease. In 1907 Dr. Stiles visited this institution and diagnosed hookworm in about twenty-five children among whom were several showing skin lesions of an unusual type. At the suggestion of Dr. Stiles thymol was given to all these patients except two who were considered too weak by the physician in charge to take the treatment. These two children had been ill for some time with a severe dermatitis on the exposed surfaces—hands, feet, face and neck—together with an exhausting diarrhœa and marked cachexia. All the other cases received the thymol and are said to have recovered, but these two died. This convinced the attending physician that others of his cases would have died but for the timely administration of thymol. Henceforth thymol was immediately given to all cases showing a similar dermatitis whether hookworm ova were found in the stools or not. The thymol was repeated weekly for six successive weeks.

This spring, while acting as physician to this orphanage, I made a diagnosis of pellagra in a number of children showing the characteristic dermatitis in mild form. When informed that the cases with this "eruption" had been regarded as hookworm disease by my predecessor and that they always improved rapidly under thymol, I called in consultation Dr. Babcock and Dr. Robt. Wilson, who concurred in the diagnosis of pellagra in about twenty-five cases then existing at the orphanage. But in order to determine the relative frequency of hookworm in the pellagrous and nonpellagrous, the stools of all inmates of the orphanage have been examined microscopically. The result has shown 26% of the total population infected with hookworm. The pellagra cases showed 29% infected. But most of our pellagra cases are among the barefooted children who possibly are more liable to hookworm infection. So far as we can judge the pellagra cases who were given the thymol for the expulsion of hookworm did not improve more rapidly than those who did not receive the thymol.

CLINICAL ASPECTS.

In both orphanages the present epidemics began in April and subsided in August. This year the disease has been of an extremely mild type, and corresponds to descriptions of pellagra as it exists now among children in Italy.

In my service the diagnosis was made chiefly upon the symmetrical dermatitis of the exposed extremities, though diarrhœa, sore mouth and changes in the appearance of the tongue were frequent. The tongue was red on the sides and on the tip, often denuded of epithelium and in a few instances the papillæ were elevated and red. But for the presence of an epidemic and the constant symmetry of the dermatitis upon the exposed surfaces many cases would not have been recognized.

The cutaneous changes began with an erythema appearing symmetrically upon the backs of the hands and arms and upon the dorsa of the feet. In some instances the backs of the hands only were involved, the erythematous border ending just above the wrists; in other cases the erythema extended over the arms, the upper limit being at the junction of the upper and middle thirds of the forearms. On the lower extremities the dorsa of the feet and the malleoli were involved, the erythema usually extending up the outer and posterior surface of the calves to within two or three inches of the popliteal space. In a few cases the backs of the forearms only or the calves of the legs only were involved. Occasionally there was a slight roughening of the elbows or knees. Casal's necklace was observed in one case. In only two instances were the unexposed parts of the body involved. One was in a girl with the fourth recurrence of the disease. The tops of her shoulders had a scaling patch the size of a dollar. In a boy with the first attack an area the size of the hand appeared over each hypogastric region. There was only one mask form, though the back of the neck and parts of the face were involved in a few of the cases. After desquamation was completed the affected surface was smooth and lighter in color than the adjoining unaffected skin. Only a few of the children complained of a burning sensation in the erythematous area. None of the cases was of the "wet" type.

The mucous membrane of the mouth, while redder than normal, lacked that fiery redness which is seen in the severe types of the

disease. In some instances the tongue was denuded in irregular areas giving the geographic aspect to the surface. Occasionally plaques of white, dead, epithelium adherent to the sides of the tongue or to the soft palate were observed.

Aside from the patella reflexes, the changes exhibited in the nervous system were few. One girl who had marked mental symptoms in her first attack five years ago had a mild eruption upon the arms and neck without other manifestations of the disease in this attack. Another girl, whose condition was being concealed from her, in an agitated manner appealed to a visiting physician to tell her if she had pellagra. She had said she would rather be dead than to know she had the disease.

In an analysis of forty-three active cases in one orphanage the frequency of the principal symptoms was noted. Thirty-three had the dermatitis upon the dorsa of the feet and the calves of the legs. These were the barefoot children. In the larger children wearing shoes the dermatitis was on the backs of the hands alone, or backs of hands and the forearms. If the shoes were left off the eruption often appeared also upon the feet, and it disappeared rapidly when the shoes were again put on, while the involvement of the hands persisted.

There were sixteen cases with frank sore mouth, eight with diarrhœa, and twenty-two with denuded and fissured tongue. It is probable that a larger number of children had slight diarrhœa which disappeared without being observed by the nurse or matrons. Hookworm ova were found in the stools of fourteen. Usually the corners of the mouth were sore.

The patella reflexes in fifty-four cases were as follows: Exaggerated twenty-eight, decreased ten, absent six, normal eight, unequal on the two sides two.

Of forty-two cases the urine showed the reaction for indican in excess of normal in 50%. The reaction was as intense in some of the interval cases as in the active ones.

On July 15th, three months after the beginning of the epidemic, twenty-nine of the nonpellagrous and twenty-nine of the pellagrous of corresponding ages were weighed and their height measured. The average weight of the pellagrous was 73 7-10 lbs., the nonpellagrous 72 5-10 lbs.; average height of former 53 10-11 in., of the latter 53 1-11 in., thus showing a slight advantage of the pel-

lagrous over the nonpellagrous, both in height and weight. Ten children of the pellagrous and ten of the controls corresponding both in height and age were weighed, showing practically the same results.

In the present epidemic no cases have been bed-ridden in either orphanage. A few have had moderate disability resulting from sore mouth and diarrhœa, but a large proportion of the cases appeared to be in excellent physicial condition. A mild degree of anemia existed among those with the hookworm complication. Several had had severe previous attacks with only a slight recurrence this year. For the most part first attacks have been severer than subsequent ones. An interval of one or more years between attacks was elicited in many cases. Of forty-three cases showing active symptoms this year seventeen have had one or more previous attacks. Of fourteen former cases without symptoms this year, three had their first attack five years ago with several recurrences, four had it four years ago and four two years ago and three one year ago.

Of eighty-five cases in the two orphanages forty-five are females and forty males. However, in one orphanage 27% of the male inmates and only 26% of the females were affected. In this orphanage of fifty-seven cases 79% were under the age of puberty. So that we are not surprised to find in these cases but little difference in the proportion of the sexes.

There have been no deaths this year, and all symptoms had practically disappeared by the first of August.

From our investigations we can say that the type of pellagra in these institutions this year is much milder than that which prevailed five or six years ago. Then a number of children had a severe form of the disease, several of whom are still in the orphanages, exhibiting only slight or no manifestations of the disease this year. In these early cases not infrequently the dermatitis was of the "wet" type. The children were confined to bed for weeks and months reaching an advanced stage of cachexia with exhausting diarrhœa and profound nervous and mental symptoms.

In 1907 two deaths, above cited, occurred. A history of these and several other cases was obtained from the physician then in charge and reported by Dr. Babcock in his first announcement on pellagra in 1907. Another death occurred in 1910. This boy was

given the usual six weeks' treatment of thymol. His skin lesions cleared up, but he then developed "typhoid fever" and finally died in paroxysms of cramps.

In all we have obtained a history of fifteen of these early cases. Thus we are able to report a total of one hundred cases of pellagra that have occurred since 1907 in the two orphanages. No doubt some cases have escaped detection. The two orphanages accommodate about five hundred children. It would not be wide of the mark to say that 20% of the total number of inmates in one of these orphanages for the past five years have had pellagra.

EPIDEMIOLOGY.

The insect life of one of these orphanages was studied by Mr. W. V. King, entomologist of the Department of Agriculture of the U. S. He kindly permitted me to give the result of his investigations. He reports the prevalence of Stomoxys Calcitrans (stable fly); Culicidæ (mosquitoes); Cimex Lectularia (bedbug); and Simulium (Buffalo gnats or black flies). The nearest running stream to the premises is three-fourths of a mile away. It was found to be infested with immature stages of Simulium. We have no expert information as to the insects at the other orphanage.

The water supply of both institutions is obtained from bored wells, one hundred feet and over deep. It is pumped into elevated tanks from which it is distributed through pipes to the several buildings.

A sewerage plant has recently been installed in one of the orphanages. In the other the open surface privy prevails, though a sewerage system will soon be put in.

The cottages in one institution are screened. In the other they are partially screened, and here the stables and stockyard are within a short distance of the living quarters and of the dining room and kitchen.

The children are allowed a trip to other parts of the State during school vacation. In one orphanage of twenty-six new cases this year seven spent from two to four weeks of the preceding summer away from the institution. Seventy children who have not yet contracted pellagra are known to have slept with those who were suffering from the disease.

Of twenty-six new cases twelve were at the orphanage during the last epidemic of pellagra at the institution in 1910, and nine had slept with one or more children who had been previously affected.

Of fifty-seven pellagrins in one institution, five are known to have had symptoms of the disease when they were admitted; twenty had been inmates for twelve months or less, thirteen for six months or less, when they developed symptoms; and thirty-two had been in the orphanage from one to twelve years before the disease was contracted. Hence, if we accept twelve months as the incubation period, twenty-five of fifty-seven cases were in the incubation stage when admitted. Or if six months be the incubation period, then eighteen had the disease on admission. This leaves thirty-two cases who probably contracted pellagra after becoming inmates of the orphanage.

ETIOLOGY.

Our limited study of the disease precludes any attempt at the solution of the etiological question; but certain predisposing factors have not escaped notice. In the first place, in orphanages we are not dealing with the average normal child. These children are descendents of parents with a short life span who in many instances have died of hereditary disease or diseases that send into the world a handicapped progeny. We have ascertained the cause of death of one parent in thirty-two pellagrous children as follows: Paralysis three, tuberculosis five, heart disease three, pneumonia five, Bright's disease two, pellagra eight, cancer one, typhoid one, appendicitis one, meningitis one, railroad accident one, malaria one. Thus 68% of these parents died of disease that transmit lowered vital resistance. Moreover, many of these children come from unhygienic environments, and have been nurtured under all the disadvantages of poverty. So that with an hereditary taint, or a lowered resistance to all diseases, what wonder that these dependants upon society should become victims of pellagra.

The age incidence in our cases is of interest. Of fifty-seven cases 79% were under twelve years when the disease developed, while only 58% of the children in this institution were under twelve years.

In both orphanages an epidemic of measles and whooping cough occurred just prior to the outbreak of pellagra. In one orphanage there were seventy-five cases of measles, in the other fifty cases.

If pellagra is contagious it certainly is much less so than measles or whooping cough or scarlet fever. Of one hundred unprotected children exposed to measles 98% have been known to contract the disease, of four hundred and one children exposed to whooping cough 91% contracted the disease, and of one hundred exposed to scarlet fever 50% became infected. In the present epidemics of pellagra the opportunity for the spread of the disease by contagion was the optimum. The children are daily in contact—in school, at play, at work, in the dining room, in the homes; and, as seen above, seventy of the unaffected children in one institution were bedfellows of the pellagrous. Yet of two hundred unprotected children in this institution only 12% contracted pellagra this year.

In one of the orphanages for the past three years only home grown and home ground corn has been used. The corn used this year is said to have been of an inferior quality to that usually harvested. Specimens of this corn were submitted to our State laboratories and also to the U. S. Bureau of Plant Industry in Washington. The report from the State laboratory gave 23 acidity for the corn. The report from Washington gave 9.5 acidity for the corn and 18.5 for the meal submitted. The Gosio ferric chloride reaction was negative. So that according to our present tests this corn was well within the limits allowed for good corn. At the other orphanage the meal and grits used are purchased in the local stores. In one orphanage the amount consumed per capita per day was 2 2-7 oz., in the other orphanage 3 oz.

In one of the orphanages cottolene has been used exclusively for over thirty years as a substitute for lard, in the other orphanage it has been used for an indefinite period.

In both orphanages the food is cooked in one kitchen and the variety is probably as great as is possible in such institutions. Vegetables are produced upon the farms in abundance and both institutions have their own dairies. However, there is a certain "monotony" of diet that is more or less unavoidable in all large institutions of this kind.

Finally we are led to inquire what will be the course of pellagra in these orphanages in the future. Will it continue to grow milder or will it vary in severity with each recurring season after the manner of other epidemic diseases? Or is there an immunizing

process acting whereby all the inmates shall become insusceptible and the disease attack only new comers?

I would here express my obligations to Dr. J. W. Babcock and Drs. J. W. and J. L. Young for professional courtesies and to the Superintendent and nurses of these orphanages for their co-operation in securing data for the preparation of this report.

NOTES ON THE EYE SYMPTOMS OF ONE HUNDRED CASES OF PELLAGRA—A SECOND REPORT.

By E. M. WHALEY, M. D., Oculist and Aurist, State Hospital for the Insane, Columbia, S. C.

In reporting these cases care has been exercised in the elimination of those pellagrins, with eye symptoms, apparently due to other causes—especially corneal involvements complicated with lues. The corneal ulcers occurring in those to which we could assign no other cause than pellagra, were large, superficial and resistant to treatment. In one case particularly did this happen and healed up only to have the diagnosis of pellagra made by the generally recognized symptoms developing rather suddenly. This case I treated two months and did not suspect the presence of pellagra, though she had mental symptoms, but I was lead off by the fact that she had been an inmate of an asylum on two previous occasions. The mental symptoms suddenly got worse and very soon after admission the development of the erythema cleared up the picture. The case of fixed globe is unique in 150 cases and would lead us to suspect syphilis on account of the immediate cause (an orbital osteitis), but we included this case as no other evidence of specific infection was found and she does not improve under mercurial treatment.

It would be highly advantageous to find one constant symptom which would point the way to early diagnosis, but this seems impossible as yet. The disease seems to attack different parts of the eye, in different years. The lids, conjunctivæ, and appendages seem to become involved synchronously with the gastro-intestinal symptoms. We find more dilated pupils than in 1909 when our previous report was made. The cases that give us most of the eye complications are those that are seen early in the attack. Later in the disease we find that pale retinæ and the lax retinal vessels are common as in all wasting disease. In every case where the accuity of vision could be gotten, the vision was below normal, the best being two-thirds and the worst for large objects. In 60 per cent. of these cases the fundi could not be examined on account of lack of co-operation of the patient. In speaking of the slow reaction of pupils to light, we mean a distinct pause after the light illumines the pupillary space before the

iris contracts. Most of the dilated pupils react slowly, but not all, and we get this sluggish action even when we find a retinitis. The nystagmus is made apparent by forced movement.

EARLY STAGES.—One case: choked disk on right side. Vision, long objects, external strabismus, plus tension left side. Pterygium, dilated pupils, chorioretinitis, which were very slow in reaction. Drooping lids. (W. L. R., 60 years of age.)

Another case of special interest (W. H. R., age 46), drooping lids, contracted pupils, quick in reaction, shallow anterior chambers, neuroretinitis, small retinal hemorrhages, diplopia, fifteen-fortieths vision. Acute general symptoms.

In taking the tension we report each eye, as the left was so frequently affected when the right was not, though the right seemed to show more changes in the fundi. The absence of corneal ulcer is accounted for by the careful hospital treatment which 90 per cent. of the patients got, the other 10 per cent. were in good circumstances and well cared for. The cornea will readily break down when the eye toilet is neglected.

In addition to the above cases we have examined fifty-six children in whose eyes there was nothing attributable to pellagra, except one, who had bilateral cataract and also had hookworms. The children all got well. This is significant, therefore, in prognosis, because when few eye symptoms exist, the disease is mild and prognosis good.

In conclusion, to summarize the two studies I have submitted upon the eye symptoms of pellagra, I may say that these symptoms are of most significance in diagnosis at the time of commencing erythema when acute inflammation of the eye structures is to be found with strabismus and irregular pupillary reactions. In the later stages the eye conditions are not characteristic of pellagra.

TABLE SHOWING RESULT OF EXAMINATION OF 100 PELLAGRINS FOR EYE TROUBLE.

Expression of lids	Good	10
	Bad	0
	Drooped	24
Conjunctiva	Conjunctivitis	9
	Appendages	2

Pupils	Dilated	40
	Contracted	5
Reaction	Slow	24
	Quick	6
Corneal Ulcer		1
Anterior Chamber	Shallow	25
Vitreous—hazy		4
Lens—Opacities		5
Retinæ	Retinitis	32
	Neuroretinitis	11
Photophobia		11
Choroditis		17
Optic Nerve	Atrophy	7
	Neuritis	17
Tension	Right—plus	15
	Left—plus	20
Muscles	Nystagmus	4
	Diplopia	5
Dilated Veins		14
Argyl-Robertson pupil		3
Reverse Argyl-Roberston pupil		3
Pterygium		1
Chronic glaucoma		1
Convulsive movement of face left side, and spasm of orbicularis on exterior fundi, which was impossible.		
Wandering eyes		1
Ataxia (Muscles)		1
Stripped keratitis		
Synchysis		
Choked Disks		2
Strabismus		4

VI. Treatment of Pellagra

THE PRESENT STATUS OF THE TREATMENT OF PELLAGRA.

By Geo. M. Niles, M. D., Atlanta, Ga.

I regret that in this study I cannot build up a logical therapy upon a proved etiology, nor can I base my conclusions upon constant and distinctive pathology.

These momentous questions are still *sub judice,* though the number of eager brains and willing hands now delving at this problem afford an earnest of its solution in the not distant future.

While, of necessity, we are waiting a definite and convincing answer to some of these etiologic and pathologic inquiries, the pellagrins are at our doors and within our gates clamoring for relief. They care not for the claims and counterclaims of the zeists and antizeists; they never heard of Sambon and his protozoan theories; and they are as little concerned for the sociologic issues involved, as for the thirty-seventh problem of Euclid. What they desire, nay, demand, is therapeutic action; and the wavering theorist who hesitates to minister to these sufferers because all is not clear, as well as the dismal pessimist, who can see nothing but defeat and death—these should take their doubtful talents into other fields, leaving this battle to the resolute and courageous spirits, who are willing to fight, even if much of the way is as yet shrouded in darkness.

I desire in this connection to submit a line of treatment, embodying suggestions from a number of observers of large knowledge, and built upon my own experience in the care of considerably over five hundred cases. This seems to be yielding satisfactory results, which cannot be explained away by the *post hoc* reply of possible critics, but which affords a reasonable inference of *propter hoc.*

This method of treatment rests upon the four basic supports of hygiene, diet, drugs and hydrotherapy, the whole of which I endeavor to permeate and leaven at all times with a hopeful and helpful psychotherapy.

The hygiene of pellagra is similar to that of other exhausting diseases, with two exceptions. Any form of alcoholic intemperance seems to exert a more malign effect than in any other malady. While an occasional alcoholic stimulant, well diluted, may find a questionable place in conditions of extreme weakness, I would hesitate to give a favorable prognosis in any pellagrin of convivial habits. I have on more than one occasion seen death quickly follow an alcoholic debauch in apparently convalescent patients.

Another hygienic precaution is the avoidance of sunlight, or even a bright light during the spring and summer months, to which may be added the danger of getting overheated. The sun's rays, either direct or reflected, possess a peculiarly irritating effect for the skin of pellagrins, the actinic power being most marked in the early spring. I have many times observed a rekindled erythema follow an exposure of less than half an hour.

A short time ago a female pellagrin under my care went in the kitchen, in the temporary absence of the cook, and prepared a single meal. She had shown no dermal signs of the disease for over two months, yet on the next day she developed an acute erythema of the hands and face.

Pellagra flourishes in hot weather, and languishes in cold weather, so whenever it is practicable to locate these sufferers in a cool environment, and keep them in it, they fare that much better.

The dietetics are somewhat different from other diseases with disordered digestion, in that the gastrointestinal manifestations are not a pathologic entity, but the expression of a centralized irritation, plus the elimination of toxins through the gastrointestinal mucosa.

Until the theory is exploded that pellagra is due to some toxic substance in either sound or spoiled corn or corn products, I feel that we are in duty bound to give our patients the benefit of the doubt by excluding such articles from the dietary.

The early diarrhœa being mainly of central origin, and to an extent compensatory, does not require a too limited regimen, nor does such seem to help the disordered bowels. The woody vegetables, and those yielding a large amount of residue, are mechanically contraindicated at any time diarrhœa is present, but care should be exercised that they are replaced by other nourishing articles. It seems that all along the course of the disease the flesh

proteins are specially well borne, and even in those where there is much gastrointestinal irritation, they agree better than in a like amount from other causes. Tender broiled steak or roast beef or mutton may be given once or twice daily; or, if the mouth is too sore to chew, either scraped beef or that ground in a sausage mill is suitable. This also applies to the white meats. Eggs are generally permissible, though in flatulent conditions it is well to use only the whites, which may be prepared in various appetizing ways, limited only by the ingenuity of the nurse. Sweet milk is valuable when it agrees, but unfortunately many pellagrins show an idiosyncrasy against it. Flatulence frequently follows its ingestion, and in some patients the stomachs furnish enough rennin to coagulate the milk promptly, but are tardy in disintegrating the curds, so there is present a sense of weight and discomfort in the epigastrium. Peptonizing the milk generally obviates this, but very few pellagrins relish peptonized milk.

The custom of certain medical wiseacres to blindly advise the daily consumption of fabulous amounts of milk and eggs, without investigating the patient's digestive ability, is calculated to make "the foolish laugh and the judicious mourn."

Fresh buttermilk, or the artificially soured milk, or lacteal champagne, is useful, seldom upsetting the stomach or intestines.

Where constipation is in evidence, oatmeal, tender vegetables (in *puree* form), thoroughly baked Irish (not sweet) potatoes, or cereals with but little sugar will aid intestinal peristalsis. During the whole course of pellagra the invalid should be nourished to the limit of assimilation, and in most instances the gastrointestinal tract will "stand for" and care for more aliment than when similarly inflamed from other diseases. The problem of bodily upkeep in pellagra should never be disregarded.

I am sorry to observe that some of our nihilistic medicos have included pellagra in the list of maladies unresponsive to drug therapy, and from their limbo of gloom we catch sundry reverberations of discouragement and ridicule aimed at the cheery optimists, who can look beyond "scar tissue," and discover some of Nature's compensatory powers. The narrow and prosaic mentality that can discern no ray of hope in the presence of trophic change or scar tissue, would deny a one-legged man the right to walk with a crutch

or artificial limb, or a congenital myopic the privilege of corrective glasses.

Permit me to briefly mention the principal drugs I now employ.

Hypodermically I use the ampules of iron arsenite solution (16 m.) and sodium cacodylate solution (¾ grain) on alternate days, injecting them under careful aseptic precautions, and giving one daily for about two weeks. After that I give an ampule every second day, still alternating them. After the acute symptoms seem to be controlled, I continue giving two injections weekly (still alternating) for several months. Frequently, when there is marked anemia, instead of the arsenite of iron, I use one c.c. ampules of green citrate of iron, each ampule containing two grains of the drug. I do not approve of the very large doses of sodium cacodylate, though some competent clinicians favor them.

Internally I use a combination of potassium iodide and Fowler's solution, in the proportion of 5 to 3. Beginning with five drops in water three times daily after meals, each day the dose should be increased one drop, until symptoms of arsenical saturation are manifested. This generally appears when 20 to 30 drops are being taken. When there is puffiness about the eyes on arising, I stop the drops for one day, beginning again at the minimum dose of five drops, and increasing as before. This procedure I continue until the eruption and sore mouth are abated, and then keep it up in 8 to 12-drop doses for several months. Should there arise a gastric or intestinal intolerance, a complication occasionally in evidence, it may be necessary to reduce the proportion of Fowler's solution to one or two in eight, instead of three as originally suggested.

For the frequent diarrhœa I have obtained satisfaction from bismuth-betanathtol and resorcin, given with milk of bismuth as a vehicle. This failing, I give tannigen, protan, or heavy doses of bismuth subgallate, or, as a last resort, powdered opium.

For the infrequent constipation either castor oil, phenolphthalein or enemas will serve, drastic cathartics being inadmissible.

For the sore mouth, a solution of thymol, one grain to the ounce of water, a little alcohol being used as a solvent, will generally prove sufficient. Also a 25 per cent. solution of boroglycerin is helpful. For the aphthous spots in the mouth or on the lips or tongue, an application of silver nitrate (20 grains to ounce of water) is in most instances efficacious.

I have ceased using stomach lavage, except in rare instances, where a great excess of sticky mucus is constantly arising.

The simple erythematous rashes on up to sloughing conditions of the hands or feet may be benefited or cured by the bland ointments, such as oxide of zinc ointment, or a 5% ointment of boric acid. Raw or weeping surfaces are soothed by a lotion of calamine and oxide of zinc in lime water, to which may be added a little rose water or other pleasant adjuvant.

For the intense burning of the hands and feet, so often and bitterly complained of, either ice-cold compresses of a mild solution of bichloride of mercury, applied at frequent intervals to the unbroken skin, or baths in hot mustard water, will afford marked relief. Two or three-grain doses of acetphenetidin, when the heart action is fairly good, will greatly aid the various neuralgic pains, while brisk rubbing of vaseline, to which has been added capsicum or menthol, is indicated for the pseudo-rheumatic pains in many joints and muscles.

After the erythema has subsided, leaving a rough and harsh surface, alcohol rubs at frequent intervals will facilitate the disappearance of this horny layer.

I do not consider that salvarsan has "made good" in the treatment of pellagra, though some still laud it in high terms.

Transfusion of blood from either healthy donors or healed pellagrins is still an available method in selected cases. Some remarkable improvements have followed its use, especially as performed by Dr. H. P. Cole, but its difficult technique, as well as other obstacles, will probably prevent its general employment.

Drainage of the gall-bladder, appendicostomy, and other surgical "stunts" have their advocates, but will hardly prove popular, the pellagrins generally being of the opinion that they would rather "bear those ills they have, than fly to others that they know not of."

Special treatment of the purely mental symptoms will not be covered here. Should such predominate, deepening into melancholia, or lapsing into dementia, the patient should be placed in an institution for the mentally sick, as these unfortunate invalids are subject to such varying moods, suicidal and otherwise, that it is often impracticable to safely care for them at home.

The effects of hydrotherapy in pellagra have in many instances proved so beneficial that some form may with propriety be invoked

in nearly every case. Hot or cold baths, simple or medicated douching, packs, moist or dry rubs, accompanied by special massage, have established their worth. These bring about increased oxidation of the tissues, more rapid elimination, greater metabolic activity, sharpened appetite, improved digestion and assimilation, and a noticeable tonic effect on the whole living organism.

Explicit directions for the different baths cannot be included in a brief paper, but will be found *in extenso* in Hinsdale's excellent work on hydratherapy. I might also say that many of our sanitariums now have well equipped departments for hydrotherapy, with expert attendants, and whenever possible it will be wise to aid in this manner Nature's efforts to eliminate this intangible, but no less consuming, toxin.

Lastly, I wish to discuss that refinement of treatment, psychotherapy, for in this we have an agent sadly neglected.

Just now, when there seems to be prevalent in our country a widespread pellagraphobia; when the uphappy victim finds most hospitals closed to him, while he is *persona non grata* in hotels and boarding houses, and where even nurses seem alarmed at its mere mention, can we wonder that the knowledge of its presence fills the sufferer with dire forebodings? Much of this phobia is due to unwise words of physicians, perhaps lightly spoken, but which make a deep and unfavorable impression upon the mentality of the already perturbed pellagrin.

Recently there came under my care a well-nourished young man with a mild case, who informed me that his family physician, on seeing the slight erythema upon his hands, remarked in an ominous manner, "Well, old fellow, you've got it." That was enough to thoroughly demoralize this patient, who at once began to conjure up images of pain and sorrow; who saw himself a pariah and an outcast, with not a ray of hope ahead. He was thinking that perhaps it would be best with his own hands to shuffle off this mortal coil, and, while in this frame of mind, I saw him.

I first assured him that his family and friends incurred no danger by his presence. I next told him that in all probability his case was curable, and by these assurances, given in a cheerful and confident manner, I gave him energy and pluck to make a fight which he had previously considered hopeless.

Though pellagra is at all times and in all phases a serious malady, we should be slow to give an unfavorable prognosis, except in extreme states.

"Apparently some regeneration may take place in diseased organs of highly organized type, if the patient's condition is kept up to the highest point of nutritive efficiency." (Walsh.)

I have in mind a young lady, who is now apparently well, who, two years ago, seemed in a hopeless condition, as far as my judgment indicated. This taught me a salutary lesson.

Certain compensatory influences may be set in motion and kept so by drugs and other material agencies, but oftener they can best be sped along by keeping the body built up and the mind cheered for a prolonged period, so that new centers may be educated, while Nature is getting accustomed to the loss of the useless ones.

I have in several instances seen pronounced psycho-neuroses seemingly arise from discouragement, from sluggish conditions developing in the bodies as a consequence of lack of hope, and from the denial of air and exercise accompanying the settled gloom of despair.

In pellagra, as in many other complicated disease pictures, there are a multiplicity of intercurrent ills coming up at frequent intervals. Many of these can promptly be alleviated, and by so doing the physician can produce in the sufferer a much more sanguine frame of mind, even if the main lesion is untouched. As one writer has fittingly expressed it, "Though nothing can be done for the disease, much can be done for the patient." It is along this line that the Eddyites, the mental healers and the quacks get their occasional spectacular results. They do not admit the incurability of any ill, but by cheerfully promising a cure, by relieving some minor discomforts, and by replacing morbid introspection with novel sensations, some invalids find their lot so much more tolerable that they know they are bettered, if not cured.

It is also reasonable to believe that by suitable suggestion we can delay, if not arrest, nerve degeneration, for a buoyant body and hopeful mind can present a firmer bulwark against the inroads of cellular destruction.

When assuming the management of a case of pellagra, the patient should be informed that very many have been cured, and that, according to the best authorities, he need not be isolated nor cast

out from those he loves. He may also be assured that strict attention to hygienic and dietetic precautions, plus other treatment instituted, will keep his body in the highest state of efficiency, and will greatly brighten his prospects. While taking cognizance of the numerous and easily managed intercurrent ills, so as to promote his comfort, we should at all times endeavor to instil a spirit of courage and optimism, so that the higher psychic centers, untrammeled by fears or obsessions, may exert their best influences over the lower centers, vegetative and otherwise.

It will demand both effort and tact on the part of the physician to keep this up, but the results will more than repay him. Even if signs of serious tropho-neuroses be evident, much can still be accomplished by cheerful suggestion and warm-hearted encouragement.

I am anxiously seeking more light in the treatment of pellagra, and should coming discoveries show me wherein I am in error, I shall gladly cast aside my old therapy for the new.

At present, however, I feel that the line of treatment herein advanced offers as much or more promise than any so far brought forward, and I lay to my soul the flattering unction that my methods are justified by tangible results, and are worthy of consideration.

PELLAGRA: ITS TREATMENT.

By E. H. BOWLING, B. S., M. D., Durham, N. C.

It is not the object of this paper to discuss the cause, pathology, or even diagnosis of pellagra; men much more capable and with better facilities have studied and will inform us of these phases of the disease.

It is my object in this paper to only deal with treatment. It occurs to me that in treating something near one hundred cases and observing them as closely as I could, that possibly I might add some little quota to our knowledge of the treatment that might be of service to some one to whom the disease was an entirely new proposition.

The treatment of pellagra is one of the greatest enigmas that we encounter in the practice of medicine; if we make the mistake of thinking that the rash observed on the hands, neck, and face *is the disease*. Because, in the first one or two seasons of the average case, this will disappear under any or no treatment, and when we pursue our line of treatment and see the rash disappear we are liable to deceive ourselves in thinking that the treatment accomplished this result; when very likely our treatment had nothing whatever to do with the favorable turn in affairs. Again we may be treating a case after our favorite line of procedure and the patient may continue to grow worse in the face of every treatment from which we expect favorable results; and when we are almost ready to surrender to the inevitable, the patient begins to improve and apparently gets well, then we are liable to give the credit to the last medicine we gave, when if we give the same treatment to the next patient, it will show no appreciable results. So we can only arrive at a remedy of real worth by giving it a long series of cases and getting favorable results in all or a very large percentage of the cases.

In the three years that the scourge had assumed any appreciable proportions in our city, I have treated nearly one hundred cases. My experience at first was the average loss of one hundred per cent. and that of my confreres was of about the same liberal proportions; but as the disease became more widespread and we had opportunities to study it more minutely, one thing I found without excep-

tion was that in all advanced cases there was a total loss of hydrochloric acid in the stomach and in fact in all my cases that were examined, I found a total absence of this acid. I see that other observers do find it present in the mild cases or in the beginning of serious cases; but in advanced cases I have never seen where any one claims that he has found the acid present. This being a constant symptom gives us a clue as to the treatment. If this is true in every case, then why? There is certainly a cause, now it is up to us to find the cause. When we can get the acid restored to the stomach in any appreciable extent, my patients always, without exception, get better; if I try to supply this deficiency by giving hydrochloride acid, it does not give me results, but rather the reverse. I find that giving the pure acid in most cases aggravates the condition.

Three years ago, I began giving chlorine water with the basic idea of getting its antiseptic effect. I had used the remedy before in treating follicular tonsilitis, diphtheria and other conditions of the fauces; I had also used it in gastric catarrhs and to sweeten up fetid breaths, and realizing that it was the strongest harmless antiseptic of which I had any knowledge, I gave it for pellagra mainly, as I say for its antiseptic effect and for the further reason that I knew nothing else to do. The first patient to whom I gave it, the effect was so magical that the patient doubted my diagnosis and I was so surprised that I really thought that I may have been mistaken. I immediately put two other patients on the same treatment and their improvement was marked from the beginning of the treatment; both got well and have had no recurrence, now three years. Since then I have used it in more than eighty cases and it invariably improves the condition if it is a recent case; in chronic cases the water alone will not meet the indications.

I have tried the experiment a great many times, of at first putting the patient on the chlorine water, letting him take it for a week or two and then stop it and give him other treatment, with the invariable result that he told me that this last medicine was not doing as much good as the other.

In treating pellagra, we should never lose sight of elimination and should keep the prima via open and as near as we can, clean. If the patient has diarrhœa, it is only an evidence that nature is making an effort to throw off the accumulated poison and we should

assist. My favorite, after trying nearly all, is castor oil. I give a tablespoonful once a day and very often keep this up for six months.

Another treatment that I have found invaluable, especially in chronic cases, is hypodermoclysis of normal salt solution. I use from one pint to one quart once a day and the effects in some cases are remarkable. With hypodermoclysis we get the antiseptic effect right into the blood and with the increased blood pressure we get a diuretic effect that is beneficial.

Cacodylate of soda in my hands is beneficial to restore the hæmoglobin to the blood and as a general tonic after the acute symptoms have subsided. I have never been able to see any benefit from its administration in the acute stages.

Urotropine and Calcium Sulphide are both valuable drugs as adjuncts, but I have never been able to get satisfactory results with them if I left off chlorine water.

It may be rank heresy to say so, but I have never seen where arsenic in any form has had the slightest effect in the treatment of pellagra, except as a restorative to the blood after the acute symptoms have subsided.

The question would naturally arise, what results does this treatment give, does it really cure? Now this is a question that is hard to answer, for pellagra is one disease that we never know when we have cured it and when we only have it in abeyance. So far my results with this line of treatment shows eighty-eight per cent. cured or apparently cured. Those patients who recovered three years ago have never seen any sign of a reappearance and their health seems in every respect to be fully restored. Some of them are heavier than they ever were and their general health seems to be above par.

The disease may return; this is a question that only time can solve, but this line of treatment gives better results in even apparent cures than any I have ever followed, and I might say better results than I have ever seen reported. It is worthy of a trial in more competent hands than mine.

CARE OF THE ALIMENTARY TRACT IN PELLAGRINS.

By A. MOULTRIE BRAILSFORD, M. D., Mullins, S. C.

Before pellagra became so widely recognized, a few peculiar cases of skin disease came under my observation that I know now were due to pellagra, but which I then thought were caused by auto-intoxication, or by some alteration in nutrition, on account of the constitutional symptoms present in each case—especially the gastrointestinal and nervous disturbances. With a simple ointment, a general cleaning out of the system, carefully regulated diet, alkaline drinks, diuretics, intestinal antiseptics, and tonics, there would be an amelioration of all the distressing symptoms. This condition apparently became permanent in a few cases, but most of them returned after variable intervals, presenting symptoms similar to the previous attack. The chagrin and disappointment of the physician was only exceeded by the grief and suffering of the patients. Under the same treatment the patients would again show signs of improvement, but I do not mean to say that they all recovered, or that none of them died.

The fact that elimination and intestinal antiseptics, a careful diet and alkaline drinks, produced an abatement of the symptoms, impressed me with the idea that the source of the trouble was in the gastrointestinal tract.

The symptoms caused by faults in diet, drugs, and diseased mucosa, are protean in character—particularly is this true in regard to changes thus produced in the skin, and, in connection with pellagra, whether we believe the disease due to poisons from food or to protozoan infection, it is interesting to note the interrelations of nutrition and the condition of the skin.

We have all observed manifold disturbances of the skin as the result of a diet producing alterations in nutrition. The skin becomes sensitive under certain conditions of diet or drugging and the reason why this reactivity develops and of what organic changes it is the expression, is ably discussed in an editorial in the A. M. A. Journal, September 21st, 1912. It appears that disturbances in the inorganic, or mineral metabolism of the body, are responsible for this condition. The fact is emphasized that "profound alterations in the dietary involving radical shifts in the types

of foods consumed may be attended by considerable changes in the so-called salt metabolism. A marked loss of mineral nutrients may ensue, for example, or, what is equally significant, the inorganic components of the organism may experience a depletion of the store of some individual element—like calcium or the alkalis, leading to a rearrangement or incordination of the ions present. Acid forming foods may lead to a shift in the usual proportions of the elements which constitute the inorganic environment of the living cells."

The experiments of Dr. Luithlen, of Vienna, to discover whether conspicuous upsets in the general inorganic metabolism will produce changes in composition of the inorganic constituents of the skin were reviewed: "Studying the proportion of calcium, magnesium, sodium, and potassium, present in the integument under radical changes of diet, or after the administration of acids, or the decalcifying oxalates, he has found that distinct chemical alterations can be detected. Sometimes it is an altered content of all the bases that is brought to light by his analysis, and sometimes a disturbance in the relative proportions of the individual ions. Here, at length, is some tangible evidence of a coincidence of general alterations in nutrition with changes in the actual chemical texture of the skin." He investigates the comparative sensitiveness of the skin to certain irritants under these new conditions and found animals subjected to acid intoxication extremely susceptible. The administration of lime in the form of calcium chlorid would relieve the irritability.

This same author experimented upon rabbits by feeding a diet of oats "deficient in calcium and acid forming in character" and found it "far more potent in producing skin sensitiveness than was a mixed diet of green vegetables."

These studies establish the fact that when alkalis are abstracted from the body fluids and tissues, a condition of irritability is induced, and that this in turn can be overcome by administering alkalis.

Since learning of the existence of pellagra in this country, I have continued to direct my energies towards the alimentary tract in every case—in many instances, arsenic has been added—but those in which no arsenic was given improved quite as rapidly as when

arsenic was used. As to comparison of the ultimate results, I have yet to await developments.

The treatment suggested consists in a careful and rigid oral hygiene. If the teeth are bad, the patient should be referred to a dentist.

The stools should be examined, and if parasites are present, proper treatment should be given for their eradication.

In addition to examining the stools, the stomach contents should be examined. Very often the diarrhœa may be due to a lack of hydrochloric acid, and in this event the administration of the acid usually checks this symptom.

To stimulate the liver and induce thorough cleansing of the bowels, calomel, sodium bicarbonate and podophyllin are given. This is followed by a stomachic and a tonic consisting of extract cod liver oil, manganese, iron, strychnine and quinine.

For fermentative dispepsia and diarrhœa, beta-naphtol-bismuth or benzo-napthtol are given.

The patient is instructed to drink copiously of alkaline waters.

As to diet—each individual case should be studied in regard to the ability of the digestive organs to care for food. The diet should be as nutritious and generous as possible. The patient should be instructed to eat slowly and masticate thoroughly. During the acute stage, with sore mouth and diarrhœa, it may be necessary to give a liquid diet exclusively. Milk, buttermilk, broths, etc., every two or three hours. But in all cases and in all stages of the disease, it is important to conserve the strength of the patient by proper nourishment.

I shall not burden you with clinical records further than to report two typical cases—one mild, the other severe—as examples which have markedly improved without the use of arsenic in any form.

Case I. Mr. R., age 38. He was pronounced a pellagrin by both Dr. Lavinder and Dr. Watson at the Pellagra Convention in Columbia two years ago. At that time there were lesions upon both hands, some stomatitis; he was considerably worried about his condition and very melancholy. His mental action was retarted, speech slow, and he possessed the typical *facies doloroso*. Upon his return from Columbia, I examined his stools, found no hookworm ova, but his stools were teeming with monads. I am satisfied he had had hookworms at an earlier age. Nearly every case of pellagra coming

under my care has been complicated by hookworms. Sambon found Ankylostoma Duodenale—the European hookworm—the most common intestinal parasites in Italian pellagrins. Roberts states: "Intestinal parasites in pellagrins deserve a more detailed study, and its importance in treatment will become more apparent in view of the wide distribution of hookworm disease in the Southern States. Either disease produces lassitude, weakness, dwarfism, anemia, emaciation, senile and wrinkled skin, dizziness, headache, gastralgia, stupid expression, and mental inertia. Pellagra is more susceptible to treatment after the removal of hookworm infection. Both diseases are rural in origin, common among farmers, and with the same general geographical distribution, often found aggravating each other in the same individual, and their association may be expected in many cases."

I gave this patient hookworm treatment in spite of the fact that there were no ova found in his stools, and followed it up with the treatment outlined above. I insisted upon his resting during the day, but as he was engaged in a large business venture, he had little time for rest. His worry over this undertaking was equal, if not greater than his anxiety over his physical condition. Handicapped by this terrible malady, and in spite of strenuous opposition in business affairs, he has carried this enterprise to a successful issue, and has lost very little time from work, and, although not a well man, he is in better health than he has been in two years. The lesions upon his hands disappeared in about six weeks after his trip to Columbia and have never returned.

Case II. Miss L., age 22. This case did not respond very readily to the above treatment; however, there was usually some response at first, but the trouble returned every year for three successive years with marked aggravation of all symptoms. In fact, they did not entirely leave her at any time—cachexia pronounced. Her mental symptoms were like those of the "Infective Exhaustive Type," her gait was slow and unsteady, but not paretic—due, perhaps, to her extreme emaciation. There were evidently no organic lesions of the brain or cord, for she has apparently completely recovered.

Of course, I am aware of the fact that the human body has a tendency to overcome all diseases that the flesh is heir to, and that in these cases it was very probably simply a matter of assisting the Vis Medicatrix Naturæ, but this would be an important procedure even if a specific had been discovered.

Corn is not allowed in any form in pellagra patients, not because I am at all sure the disease is due to corn, but because it has been incriminated more than any other one thing as the cause of pellagra, and I do not care to take chances.

To anti-Zeists, the contention that pellagra cannot be due to a fungus growing on corn will be established by the fact that the disease has only become prevalent within recent years in this country, although corn has been eaten here for nearly three centuries. Besides, corn is also eaten to a large extent in cities, and pellagra is a disease of the rural districts, and it is reported that it sometimes develops in persons who assert they have never eaten corn.

Upon the other hand, the Zeists can contend with equal vehemence that corn is responsible for the existence of pellagra, for previous to thirty years ago there was not as much corn brought from the West as at the present day—especially in a ground state. Meal is shipped in sacks, and when exposed to rain, or becomes wet, it cakes and ferments. Speculators in corn store the grain in warehouses where it sweats and moulds while awaiting a "rising market." Besides, the Commissioner of Agriculture of South Carolina, Mr. E. J. Watson, asserts that quantities of this corn is damaged and has demonstrated its toxic properties by experiments upon rats and other animals. Then, again, some of our farmers do not wait until late fall to harvest their corn after it matures and dries upon the stalk, but cut the stalks before the ears ripen and "shock" them in the field.

Therefore, whether pellagra is due to corn or to a protozoan infection, it is well to avoid the possibility of introducing a poison into an already damaged intestinal tract, and whether the condition of the intestinal tract is due to some local irritation primarily, or is secondary to some nervous origin, the demand for treatment along this line is none the less urgent.

I do not wish to convey the impression that I never use arsenic—in some cases I use it freely—or that I imagine the source of the malady is in the bowel, and that the only way in which to treat pellagra is to attack it in the alimentary tract, but certainly the earliest symptoms are manifested there and they are the "most persistent and the most dangerous of all pellagra symptoms." I simply wish to add my very limited experience to emphasize the importance of careful attention to the conditions present throughout the entire alimentary tract in every case of pellagra.

THE TREATMENT OF PELLAGRA BY DIRECT TRANSFUSION OF BLOOD.

A Review of Thirty-four Cases, By H. P. COLE, M. D., Mobile, Ala.

The transfusion method of treatment in pellagra originated with me through an opportunity to transfuse an insane pellagrin at the Mt. Vernon Insane Hospital, Mt. Vernon, Alabama, on August 4th, 1908. Encouraged by the immediate improvement and rapid recovery in this patient, I have since transfused thirty-three additional patients in the terminal stages of the disease.

We have endeavored to preserve a spirit of skepticism and unbiased judgment throughout our investigations, and to draw accurate conclusions from the data presented.

Transfusion has been resorted to only in cases in the last stages of pellagra, or steadily retrograding under prolonged and careful treatment by approved therapeutic measures. To illustrate the type of cases in which transfusion has been employed, it is sufficient to state that two patients were moribund at the time of operation, and one patient died on the railway train twenty minutes before arriving at Mobile for transfusion.

	Cases.
Transfused	34
Females, aged 22-64	25
Males, aged 3-48	9
Recoveries (64.7)	21
Deaths (35.3)	13

	Cases.
Temporary improvement followed by death	4
No improvement following transfusion	9
Complications incompatible with recovery	3

Patient 1, a male, aged 42, whose case was complicated with tuberculous peritonitis, showed temporary improvement for several days, but died one month after the operation.

Patient 2, a male, aged 3, showed distinct improvements following transfusion, but died eight days later from intestinal perforation.

[1]The case I reported as relapsed, before the British Medical Association in July, 1911, was found to be unrelapsed—now over five years after transfusion.

Patient 3, a male, aged 16, had bilateral pneumonia, at the time of transfusion; no improvement; died one week later.

	Cases
Complications presenting insufficient flow of blood, followed by death	2

In Case 1 the only available donor permitted insufficient transfusion through a severe degree of arterio-sclerosis. In Case 2 inadequate operative surroundings and a neurotic fourteen-year-old boy as the only available donor permitted insufficient transfusion.

	Cases
Patients moribund at operation, followed by death	3

It will be noted that five out of the thirteen cases in which death resulted might well be excluded, for the following reasons· Two patients received an inadequate amount of blood at transfusion, and three were moribund at the time of operation. Excluding these five cases, the mortality rate would be 23.4 per cent., as compared with 35.3 per cent. in the entire series. Considering the grave mortality rate in the type of patients on whom transfusion was performed, we can but feel that our mortality rate of 35.3 per cent. in the entire number of cases compares most favorably with the mortality (80 or 90 per cent.) in this type of cases treated by other therapeutic procedures. We have been unable to observe that transfusion was a direct factor of death in any of the cases; the deaths followed in periods of from three hours to one month after operation. One patient manifested symptoms of cocainism, necessitating a termination of transfusion at the end of fifteen minutes. Syncope has been noted in two donors; in one, an anterio-sclerotic individual, at the end of eighteen minutes; the other, at the end of twenty-four minutes, in a young man, after undue exertion. This patient, however, made an excellent recovery from pellagra. Neither hæmolysis nor agglutination, thrombosis nor embolism, have been observed in any of the cases.

All the recovered patients presented distinct and severe lesions of pellagra; there were marked emaciation, asthenia, reflex excitability, and in many cases grave mental changes. Severe pellagra erythema, stomatitis, and diarrhœa were present in a majority of the cases. Within a few days after the transfusion in the recovered there were either alleviation or disappearance of all the symptoms

of pellagra; there was a rapid disappearance of the pellagra erythema, stomatitis, and diarrhœa, and also a gradual alleviation of the mental and nervous symptoms. In several cases there was an astonishing improvement in the patient's mental condition shortly following operation. In all the recovered cases there was rapid increase in the patient's hemoglobin index, a rapid return of body strength, a return of digestive faculties, and an increase of body weight. All the recovered patients gained from three to eight and one-half pounds in the first week following transfusion, one patient gaining thirty-four pounds within eleven weeks. All the recovered patients have returned to a normal condition within from one to four months after operation; several are in better physical condition than they have presented for years.

It is but just to state that all approved therapeutic procedures were employed in the recovered cases, both previous to and following the operation. As these procedures were employed without beneficial effect previous to the operation, it is fair to assume that they were unimportant factors in the recoveries after transfusion.

We have been unable to ascertain a constant clinical sign that would indicate a certainty of recovery following transfusion. A moribund state of the patient and cases of pellagra with grave pathologic conditions, cardiac, renal or pulmonary, contraindicate the employment of transfusion. The necessity of resorting to transfusion can be ascertained only on the appearance of positive signs of retrogression under approved institutional and constitutional therapeutic agents.

A majority of the patients referred for transfusion have recovered through hygienic, supportive treatment, not necessitating the employment of transfusion.

Transfusion, itself a delicate procedure, should be attempted only by those experienced in the technique, in adequate surroundings for its performance, and with the proper post-operation treatment.

In these transfusions we have endeavored to employ donors who have lived in the same environment as the recipients, assuming that such donors who have not contracted pellagra possess a certain degree of immunity.

Transfusion was restorted to from donors who have recovered from pellagra in three cases; recovery occurred in one case (33 1-3 per cent.).

Transfusion was made from donors who had never had pellagra in thirty-two cases; recovery ensued in twenty cases (62.5 per cent.).

We assume that there is at least no preference of a donor who has had pellagra over a donor who has never had pellagra.

Transfusion was resorted to from donors who were relatives of the patient, but who has never had pellagra, in seventeen cases; recovery occurred in twelve cases (70.5 per cent.). Transfusion was made from donors who were not relatives and who had never had pellagra in fourteen cases; recovery in eleven cases (78.5 per cent.). Here we may assume, at least, that there is no ground for preference of the use of a relative over the use of a nonrelative.

We are unable to state from the statistics available that there is any immune principle transferred by transfusion. It is probable that any beneficial results obtained may be attributed to the relief of the existing anæmia, permitting the patient's organism to approach its normal functional activities, and thus to combat the progress of the disease.

CONCLUSIONS.

In transfusion in thirty-four cases of pellagra we have found no ill effect resulting to the patients directly from the operation. We may safely resort to transfusion in the severe type of case, steadily retrogressing under approved therapeutic procedures, with the knowledge that improvement or recovery will occur in a majority (64.7%) of these resistant cases. We have noted no advantage in the employment of a donor who has recovered from pellagra as compared with the donor who has never had pellagra.

There is apparently no advantage in the use of a relative for a donor as compared to the use of a nonrelative.

The recoveries (64.7 per cent.) following transfusion in the grave type of cases compares most favorably with the recoveries (10 to 20 per cent.) in the same type of cases in which other therapeutic measures are employed.

The employment of transfusion in the terminal stages of pellagra must be undertaken with a full knowledge of the difficulties and dangers of the operation. Without careful selection of the cases and unprejudiced conclusions this procedure will fall into an undeserved ill repute.

202-204 Conti Street.

THE RELATIVE VALUE OF SOAMIN AND SALVARSAN IN THE SPECIFIC TREATMENT OF PELLAGRA.

By E. H. MARTIN, M. D., Hot Springs, Ark.

That pellagra is of comparatively recent occurrence in our practice must be the excuse for the small number of cases on which my deductions are based. Written histories and records have, however, been kept of each case and these, eighty-three in number, have been carefully reread, analyzed and classified and all cases in which the diagnosis was doubtful or which were under treatment only a short time have been excluded in the final analysis. This has excluded a number of apparent cures and brings the final series down to cases in which the diagnosis was absolutely positive and which, except the fatal cases, each had sufficient treatment to exclude chance or accidental recoveries.

Of the eighty-three cases four came first under observation in 1909, nine in 1910, thirty-five in 1911 and thirty-five in 1912. These figures do not show the relative frequency of the disease in Arkansas during those years, as the patients came from many States, and the lack of increase in 1912 over 1911 merely argues that fewer pellagra patients are leaving home for treatment.

A very careful analysis of these records has caused me to exclude forty-five on account of the data being insufficient for certainty. These forty-five cases were treated for a short time with soamin in some instances and some others had single doses of salvarsan and almost all of them recovered, but the cause and effect are not absolutely certain and they are therefore not offered as evidence. Some of the forty-five are also still under treatment.

Of the thirty-eight others, eleven come from the soamin series and twenty-seven from those treated with salvarsan.

The eleven cases sufficiently treated with soamin give nine recoveries and two deaths. Of the nine recovered there were two who received single doses of salvarsan, but the soamin treatment preponderated. Each patient received many doses of soamin and treatment was kept up in most instances over two summers. One of the recovered cases dates from 1909, four from 1910, and four from 1911.

Of the two fatal cases one died of chronic nephritis, the other from cerebral complications probably made worse by the slight reaction sometimes following soamin in very severe cases. This idea will be discussed later.

Of the twenty-seven cases taken from the salvarsan series, twenty show apparent cures, three are doubtful but greatly improved and four died after treatment was begun.

Of the twenty presumed cures, seven were treated in 1911 and remain cured. Four of these came back and received midwinter doses of salvarsan, which may or may not have been necessary. There were thirteen seemingly cured by salvarsan in 1912, of whom nine were discharged previous to August 1st and are still well. These twenty cases and the three doubtful ones received the following number of doses: Four received five doses each, twelve received six doses each, two received seven doses each, three received eight doses each, one received ten doses and one received twelve doses.

These doses were usually given at intervals of from seven to ten days and the first dose was usually .2 gram, the second dose .4 gram, and the subsequent doses whatever the patient's weight called for—basing the full dosage on .1 gram for every twenty pounds after allowing for clothing.

In very weak and nervous cases these doses are reduced. Each of these patients received the number of doses mentioned in an unbroken series except the two getting ten and twelve doses. The former of these was given four doses at one series, four at a second series and two at a third. The latter received three doses at first, three doses several months later and six doses in her third series. The reason in each case was the same—not enough treatment at first because we were in unknown territory and did not know how many doses could safely be given at short intervals. Both cases are apparently cured. Of the three doubtful cases two were given six doses each and one received eight doses. They apparently recovered and lost pellagrous symptoms, but each had to leave Hot Springs before receiving a dose without a subsequent reaction. These three patients may be really cured, but as this reaction seems to be proof of the presence of the organism causing pellagra the patient can not be regarded as cured until a dose of salvarsan can be given without a reaction following.

The author of this paper has met with strong opposition in advancing the claim that the reaction following the administration of salvarsan in cases of syphilis and pellagra is due to toxines released from killed organisms causing those diseases. However, opposition can not alter facts—the reaction, consisting of fever, emesis and bowel movements of a watery and gaseous character, does occur. Either of these three factors of the reaction or any two of them may be absent or all may be present, in either case the reaction is positive. Granting that the distilled water is fresh and the technique of administration all that it should be this reaction does *not* occur in any patient *not* having lues or pellagra. That it is sometimes absent in certain cases of syphilis is at times explained by the organisms not being in reach of the circulating blood and in other cases its absence can not be explained in the light of our present knowledge though certainly there is a reason which we will some day understand. However, it is rarely absent except in cases where its absence can be expected—after first doses in tabes or spinal syphilis for instance. So certain are these facts in my opinion, an opinion based on carefully watching and recording the results of 1,100 intravenous doses of salvarsan, that my guide for treatment in both syphilis and pellagra is the reaction. Each patient is given an appropriate intravenous dose usually seven days apart until no reaction follows—meaning no rise of temperature above normal, no emesis not otherwise explainable, and no characteristic bowel movements. A single watery, gaseous bowel movement constitutes evidence of reaction and calls for another dose as imperatively as a rise of temperature. This absence of reaction which should indicate a total destruction of the germs of the disease is attained in 70% of all cases of syphilis by two doses if given within 10 days, 28% require three doses at that close interval and 2%, mostly cases of cerebral or spinal syphilis, will require four or five doses. Pellagrins, however, require from five to eight doses to cause the reaction to disappear, as a rule, though apparent cures often occur after one dose.

Also, in cases of cerebral and spinal syphilis there is often seen a delayed reaction, never seen in other cases of syphilis. So, knowing from the clinical symptoms of pellagra—the increased reflexes, the nervous and mental symptoms, the symmetrical character of the skin lesions, that the spinal cord and the brain are the chief sites

of trouble, we would naturally expect some such prolongation of the reaction following salvarsan as is at times seen in lues of the nervous system.

Such is invariably the case, the reaction of salvarsan in cases of pellagra is not a frank paroxysm as it is in cases of secondary syphilis, but is usually a matter of three days. The reason for this is not difficult to imagine, though it may not yet be possible to prove. If the organisms, doubtless spirilla or spirochetes, are located in the nervous system the circulating blood can not bear its salvarsan to them with sufficient freedom to cause their destruction in situ, but it is probable that sufficient approach is made by the salvarsan bearing blood to influence the breaking up of colonies and to cause the organisms to pass gradually into the blood current where they are killed from day to day until so much salvarsan has been eliminated from the patient that it is no longer effective.

The fact that colonies of organisms are thus broken up was sufficiently proven to several patients by the appearance of acute symptoms. For instance, in one case the second dose of salvarsan, while improving existing symptoms, caused a renewal of stomatitis. In another case, the skin lesions present rapidly disappeared, but an entirely new set of symmetrical skin lesions followed the administration of the drug. These were, of course, temporary and yielded to later treatment. In a great many cases the increasing of the diarrhœa shortly after treatment is begun is very noticeable, both in soamin cases and those treated with salvarsan. Analogous to this, I have seen similar results in tertiary syphilis in at least a score of cases. Patients with strictly tertiary lesions and with presumably not a single spirochete in the circulating blood, would be changed to secondary cases after the administration of a dose of salvarson as shown by the prompt appearance of a secondary eruption which, however, would disappear after or even before the next dose.

The severity of this reaction depends upon the number of organisms killed and therefore upon the severity of the particular case and also upon the size of the initial dose. It is reasonable to suppose that there are usually germs of pellagra in other parts of the patient's body, in the blood for instance, even if the central colonies are in the nervous system. Therefore, a very desperate reaction may be expected in some cases, though not all, if the first dose be a full one.

It is much more desirable to give small and increasing doses and not give a full dose until the third, as then the free germs in the system may be presumed to have been already destroyed. Even with this precaution there is danger in cases with marked cerebral symptoms, which brings us back to our four deaths. Three of these were cerebral cases, practically insane, the fourth gave no mental symptoms but was a chronic alcoholic, as were two of the other three. These cases were given extremely small doses of salvarsan, but there seemed to be some connection in each of the three cerebral cases between the reaction and a subsequent cerebritis or meningitis. One of these, a woman, was given only one dose of .150 gram and while she improved wonderfully for three days, she could not sleep. Two days later she died with meningitis. The other two cerebral cases had similar histories, except that they were also alcoholic habitues, and the withdrawal of whiskey, voluntary and persisted in, may have had some influence in bringing on cerebritis and coma. The fourth fatal case was a very constant drinker and his cerebritis also followed his refusal to drink even moderately. His reaction was ten days past and he had been out on the street several days before he began to have nervous symptoms and what appeared to be an acute attack of pellagra was precipitated. This came with fever, eruption, diarrhœa, sore mouth and mental hebetude which deepened from day to day until coma supervened on the 15th day and death on the 16th. Eminent consultants considered his death to be due to alcoholism, but it seemed to me to be a pellagrous explosion. The other three cases were close to the end and it may be that no possible delicacy of approach could have saved them, but it is equally as possible that they might have lived a few days longer but for the reaction following the salvarsan, which is also true of the case previously mentioned which died during the treatment with soamin.

Comparing final results from soamin and salvarsan, there seems to be but small choice between them. Each seems to entirely cure the cases completely treated. So we must weigh the two plans of treatment for other advantages. Soamin must be given hypodermatically from three to five days apart for from eighteen months to two years, allowing a three weeks interval between each course of 100 grains; this is laborious, but it is at least possible anywhere and intravenous medication is not. For this reason alone the

soamin treatment will probably be the most used in rural districts where distilled water can not be procured fresh from the still and where the intravenous needle is not required often enough for the practitioner to acquire sufficient skill to administer repeated doses in the same spot without injuring the vein, often the only available vein and needed for future doses. On the other hand the early results from soamin are extremely slow compared with the almost miraculous disappearance of symptoms in the majority of cases after using salvarsan—and many cases are so slow to begin to improve on soamin that the patient and the physician both become discouraged.

The average patient will take six doses of salvarsan in five weeks and be cured thereby and that is evidently preferable and should be the course pursued whenever the patient can be so treated or can reach such treatment. Some patients can only afford to remain away from home about two weeks, long enough to get three doses. When that is the case it is well to give them that much intravenous treatment and then have the soamin kept up after they get home. With two such specifics which will absolutely cure practically all cases not rapidly approaching the grave it is time for the physicians of America to cease thinking of pellagra as an incurable disease.

That we can not save every patient should not discourage or lend doubt. We do not save every patient who has malarial poisoning, yet no one doubts the specific value of quinia. We readily understand and appreciate the fact that one may be provided with a perfect weapon or instrument and not know how to use it. Improperly used every such agent—from a fourteen-inch gun to a capsule of quinine—is a failure. The fact that repeated failures to really cure pellagra even when the way has been pointed out, is no more surprising than the fact that many a case of malarial fever follows the bungling use of a proven specific.

On the other hand thousands of cases of pellagra have been left to run their courses downward merely because the physicians in charge refused to believe the facts stated in this paper, facts which were offered to the profession with equal clearness if not with as much proof one year ago. Thousands of cases of pellagra are being permitted to go on without any attempt whatever to use any specific treatment. Hundreds of these unfortunates are in institutions

offering facilities for any kind of treatment and paying good salaries to educated and trained men to give these patients the best.

Are they doing their duty? Are the physicians of the South who are waiting for more proof before trying specific treatment, while a large percentage of their patients are dying, entirely blameless?

Dugan-Stuart Building.

THE USE OF SALVARSAN IN PELLAGRA.

By DR. W. J. CRANSTON, Assistant Physician State Sanitarium, Milledgeville, Ga.

Early in the year 1912 we reported eleven cases of pellagra in colored females to whom salvarsan was administered in 1911 at the Georgia State Sanitarium. In that paper we reviewed briefly the number of remedies used before salvarsan was given and their failure of result, among them being atoxal, bichloride of mercury, urotropin, calcium sulphide, sodium bicarbonate and pancreatin. We expressed the opinion that drugs had been useless. That paper was necessarily brief because of the few cases to whom salvarsan had been given, and the opinion expressed was not final. We stated that we hoped the following year's work would clear up the atmosphere. Our results at that time were as follows:

Of the eleven cases treated 18% recovered; 9% remained unimproved; 36% relapsed and 36% died. The status of those cases one year after treatment is interesting and given herewith.

One case remains perfectly well; one case recovered; was permitted to go home and we have not heard from her. Four cases died; two cases relapsed and died; two cases relapsed and are still ill September 20th, 1912; one case relapsed and recovered, or 9% recovered without relapse; 9% recovered and no subsequent history; 36% died without improvement; 18% relapsed and died; 18% relapsed and are still ill, and 9% relapsed and recovered. Stated differently, 18% recovered; 9% relapsed and recovered; 55% died; 18% are ill again.

Despite the discouraging results obtained in 1911, we felt impelled to give salvarsan a more thorough trial because of the glowing reports recorded by other observers in its use. Beginning January 1st, 1912, we determined to treat with salvarsan all cases in the colored female department admitted to the Georgia State Sanitarium suffering of pellagra, and all colored females that should develop pellagra during that year. During that time sixty patients have been admitted with pellagra, or have developed pellagra here. The treatment given was as follows: .3 gm. salvarsan diluted to 125 cc. saline—prepared as per instructions contained in the wrappers—was injected into the veins on the 1st-10th, and .6 gm. diluted to

300 cc. saline on the 20th day of treatment. Other treatment was purely symptomatic, such as diet for diarrhœa, codeine or morphine for pain; strychnine for weakened heart action, etc. In a few cases a fourth injection of .6 gm. was given when there was not sufficient improvement after the third dose.

The most prompt effect seems to have been manifested upon the intestines. In a great majority of cases the diarrhœa subsided promptly. Of the sixty cases reported, in forty-one the diarrhœa was checked and the bowels remained more or less constipated, but diarrhœa returned in four of these cases. In five of the remaining cases there was improvement, but in one of the latter the improvement was only temporary. Twelve cases showed no improvement at all. In two cases diarrhœa repeatedly returned.

The skin symptoms, where we would expect the most spectacular results, were not so encouraging. Twenty cases showed complete recovery from the skin lesions with one relapse. Twenty cases showed marked improvement; in two cases very little improvement; eighteen cases were unimproved at all. One case improved, relapsed, grew worse; one case cleared up entirely and subsequently developed the skin lesions again.

The result obtained in the tongue and mouth symptoms were decidedly more vague. In fourteen cases the inflammation involving the tongue and buccal cavity cleared up entirely. In twenty-two cases there was absolutely no improvement. Twenty-four cases improved a great deal but still show slight symptoms, such as inflammation around the margin of the tongue, indentation of the tongue, fissures and pallor.

Marked nervous symptoms were absent in all but six of our cases and five of the six died; in the one who survived, the nervous symptoms have disappeared.

The effect on the mental symptoms was practically nil.

The effect upon the general nutrition was striking in some instances, ten cases being in excellent physical condition at present; ten being in very good physical condition; nine being well nourished, six being only fairly well nourished; twenty-two being very poorly nourished, and in one case there has been apparently no effect whatever upon the general nutrition.

Ascaris Lumbricoides complicated four cases, two of whom improved and two died, Tuberculosis complicated eight; five recov-

ered; one improved and two died. Nephritis complicated three cases, all of whom died. (Nephritis probably a sequela and not a complication.) Two cases were epileptic, both of whom recovered from the pellagra.

Four cases were among the group treated in 1911 who had relapsed. Two recovered after the 1912 treatment and have since relapsed and the third relapsed later; one partially recovered and relapsed and one died.

It was the initial attack in thirty cases; the second attack in twenty-four cases and the third or more in six cases. Of those who had had one previous attack, four had been treated with salvarsan in 1911 with recovery. The others had recovered from their former attacks of pellagra without the use of salvarsan.

We were unable to draw any conclusions from the reaction, most patients reacting from one to three degrees temperature within twenty-four hours, and generally after the third dose there was nausea and vomiting.

We found no contraindications to the use of the drug.

As to results of nine months' treatment, twenty-two recovered: ten partially recovered; seven were not benefited in the least; twenty-one died; three relapsed. In nearly all cases, except in relapses or deaths, the general state of nutrition shortly after the treatment has remained practically the same until the present time—September 20th, 1912. Where it was very good it has remained so; where it was poor it has not improved.

Among those who died one lived three months after the last dose of salvarsan and one died the same day. Given in weeks, four lived less than one week; six lived one week; one lived two weeks; one lived three weeks; one lived one month; four lived six weeks; two lived seven weeks; two lived two months; one lived nine weeks; one lived ten weeks and one lived three months.

On the face of it that does not seem so bad, and yet when we study these figures what do we find? Why, that of the sixty cases treated with salvarsan in nine months' time 36% recovered; 16% improved; 12% were not helped and 35% died.

During the same period of time eighty-six cases were reported in the white male and female and colored male wards. Of these eighty-six cases 33% died. None of these cases were treated with salvarsan and yet the mortality was 2% lower than ours.

These eighty-six cases analyzed further, show a very interesting ratio.

Thirty-two cases were received in the white female ward and 31% died.

Thirty-eight cases were received in the white male ward and 29% died.

Sixteen cases were received in the colored male ward and 50% died.

This is of particular interest because the nursing in the white female ward is quite the most, and in the colored male ward decidedly the least, efficient. Bearing this fact in mind the mortality then apparently bears an inverse ratio to the efficiency of the nursing corps.

A review of the cases on or about October 1st, 1912, show that of the thirty-nine survivors of the original sixty cases fourteeen have either relapsed definitely or show symptoms of pellagra, such as colicky pains in abdomen, diarrhœa, inflamed tongue or buccal mucous membrane, or thickened, roughened and darkened areas over the extremities.

Conclusions: Realizing the gravity of expressing an adverse opinion of a drug that might be of benefit to this class of patients, we have hesitated in expressing an opinion. However, based upon the facts as above stated, our conclusions are as follows:

That salvarsan is not a specific in pellagra. Its apparent beneficial effect upon the symptoms we believe to be purely coincidental. We have seen cases of pellagra clear up as readily under other treatment as under salvarsan. Some of the cases were absolutely uneffected and some grew worse under treatment. Of thirty-nine cases surviving fourteen cases show evidence of relapse.

That salvarsan acts as a general tonic.

That the best results to be obtained in the treatment of pellagra are through careful and conscientious nursing.

That the only constant factor in the use of salvarsan is the expense.

We wish to express our appreciation to Dr. P. H. Weeks, who either assisted us in administering, or himself administered, the salvarsan to the majority of these patients, and to Nurse Ruth Price for her assistance in note taking.

A FEW CASES ARE SUBMITTED HEREWITH.

N. A., No. 1. Middle age, colored female; rather poorly nourished. Was put to bed April 24th, 1912, and treated for Ascaris without result. The treatment was repeated May 2d. On June 8th she was constipated and there were slight skin symptoms of pellagra. The buccal symptoms were mild. On June 10th there was nausea and vomiting. On June 13th and 21st she was given salvarsan, following which the skin, tongue and intestinal symptoms seemed to have improved. On July 1st, a third dose of salvarsan was given. On July 29th all skin symptoms were growing worse and more extensive. There was nausea, vomiting and severe diarrhœa. The tongue and mouth were decidedly worse and there was salivation. The patient was emaciated and prostrated. A fourth dose of salvarsan—.6 gm.—was given on this date. On September 9th there had apparently been no improvement in her condition whatever. On September 20th her general condition remained the same.

In this case salvarsan seems to have been fruitless. Within twenty-eight days of the last treatment all symptoms were markedly worse despite the fact that early in the treatment she improved. A fourth full dose of salvarsan seems to have been equally fruitless and until other treatment was instituted she grew steadily worse.

E. J., No. 33. Poorly nourished colored female; young adult. Slight symptoms of pellagra on May 19th, 1912. Was decidedly worse on June 1st. Positive diagnosis of pellagra was made. Salvarsan was given June 3, 1912. On June 12th the intestinal symptoms were improved. Salvarsan was given again June 13th and 22d. Tongue improved, but the patient was emaciated, gradually grew worse and died August 24th, 1912.

B. A., No. 2. Colored female, age 29. First attack possibly in the spring of 1911, with complete physical recovery. Second attack in the fall of 1911, from which there was not entire recovery, and in the spring of 1912 she suffered a third attack. Skin symptoms were quite distinct. The tongue was raw and the bowels were constipated. She was very thin. One week after the first dose the skin symptoms improved, but the tongue appeared no better. Two weeks later there was no change. After the third dose there was nausea and vomiting. The skin symptoms improved, but the tongue grew no

better. One month later there was slight general improvement. By the middle of August the general condition was much improved and the skin symptoms practically clear. On September 2d there was marked abdominal pain, with tenderness and rigidity, lasting three days, which cleared up under castor oil. On September 20th there was no evidence of pellagra except the tongue was pale and indented. Developed tuberculosis about this time.

This case cleared up from the first attack without the use of salvarsan. Improvement after the second attack was marked, though there was not complete recovery. Patient then cleared up almost entirely after the use of salvarsan in the third attack.

F. D., No. 3. Middle age, colored female, presenting the first symptoms of pellagra July 5th, 1912, when the tongue and skin symptoms were pronounced and there was mild diarrhœa. Salvarsan was given July 10th-20th and 30th. On the latter date the skin was much improved, the bowels normal and the tongue decidedly better. On September 6th the skin was much improved, but there was still evidence of its involvement. There was silght diarrhœa and slight tongue involvement. On September 20th her condition was good though these slight symptoms, excepting diarrhœa, persisted. This case will probably clear up entirely.

C. B., No. 7. Middle age, colored female. On March 25th, 1912, patient developed severe symptoms of pellagra. Salvarsan was given on March 28th. On April 2d the tongue was no better, though the skin symptoms improved slightly. A second dose of salvarsan was given on April 8th. On April 16th the skin and intestinal symptoms seemed better. Final dose was given on April 18th. On the 23d the bowels were normal, but the tongue and skin symptoms seemed to be spreading, and the mouth was decidedly worse. Patient grew worst rapidly and died.

The skin symptoms improved and the bowels were normal five days after the last treatment. The tongue never improved at any time and patient died a few days after the last treatment.

A. C., No. 11. Well nourished, middle aged, colored female, with severe diarrhœa, extensive skin lesions and very much inflamed mouth; acneform eruption on face, spastic gait, inco-ordination, headache and vertigo; tenderness over nerve trunks; general tremor; impaired speech. Was given salvarsan April 11th, 1912. Bowels became constipated. April 21st had diarrhœa. She was given

salvarsan again on May 2d for the third time; was constipated. At this time she was unable to walk. On May 15th the nervous symptoms were no better; growing weaker. June 11th the skin, tongue and nervous symptoms seemed to improve, but she was evidently decidedly worse and died June 17th, 1912.

This was the very worse form of pellagra, and while at one time there was slight improvement in the symptoms, the patient gradually grew worst from the first.

B. F., No. 18. Well nourished, colored female; young adult. On February 23d, 1912, was excited; legs edematous. On March 13th suppression of urine, followed by diarrhœa. The tongue was very red and the skin symptoms were extensive. Lumbar puncture showed considerable amount of blood. Was given salvarsan March 16th, 1912. Was no improvement on March 19th. A second dose was given March 30th. On April 3d there was very slight improvement. The last dose was given April 9th and she died on the 16th, never having improved very much at any time.

O. F., No. 46. Middle aged, colored female; well nourished. August 6th, 1911, developed pellagra. Was given 606; improved and was supposed to be entirely well; relapsed March, 1912. Was given 606 April 1st-11th and 19th, 1912, which was followed by nausea and vomiting. Bowels became constipated, but the skin symptoms were unaffected; the tongue grew worse. On May 13th she attempted suicide. On May 22d was constipated and the tongue was not improved. On June 6th the general condition was better. On July 30th the tongue was worse; skin symptoms returned worse than in the last attack and there was diarrhœa. On September 6th there was improvement in the skin symptoms but the tongue was no better. The general condition was good. September 26th she appeared to be losing ground and looked weaker.

This patient recovered after the first attack, when she was given 606. She improved very much after the second attack, but has relapsed again.

M. J., No. 27. Colored female; young adult. Poorly nourished. July 29th, 1911, there were slight symptoms of pellagra and she was given 606. There was no improvement until the fall of that year; then she grew much stronger, and on the 8th of May, 1912, there was no evidence of pellagra. The 10th of May she became ill;

on the 29th of May pellagra had undoubtedly appeared again. On the 28th of June, 1912, she was given salvarsan, which was repeated on the 8th of July and again on the 18th. She never improved at any time and died July 22d, 1912.

There was marked improvement several months after first treatment, but died four days after the last dose in the last treatment.

M. B., No. 4. Colored Female, age 21. Deaf mute. Epileptic. In December of 1911 extensive skin involvement without tongue or intestinal symptoms. Patient recovered entirely without the use of salvarsan. On May 22d she developed marked skin, tongue and intestinal symptoms and was very much emaciated. Salvarsan was given May 23d, June 1st and 11th. On June 12th the skin symptoms were improving nicely, but the tongue was no better. On July 1st all symptoms had entirely subsided. On September 6th there were no symptoms except the lips were slightly inflamed. In the meantime this patient had developed tuberculosis.

This case probably recovered entirely from the attack in the winter of 1911 without the use of salvarsan and then cleared up again from the attack in the spring with the use of salvarsan. It is strongly probable that the inflammation of the lips is the return of her symptoms.

N. B., No. 6. Colored female, age 25. Patient had a mild attack in the fall of 1911 from which she recovered. On April 9th, 1912, a second attack occurred. Salvarsan was given on April 23d, 1912. The bowels improved slightly, but the tongue and skin symptoms remained the same and she became more feeble. On May 3d, 1912, a second dose of salvarsan was given. The diarrhœa was very severe on the 3d, 4th and 5th, and on the 7th salivation was marked. On the 13th final dose was given, following which there was no improvement. On May 22d the bowels became normal, but the patient grew steadily worse and died July 4th, 1912.

This case recovered from a former mild attack without the use of salvarsan and then succumbed despite the use of salvarsan in the last attack.

M. W., No. 51. On July 23d, 1912, patient developed marked symptoms of pellagra. Was given salvarsan July 23d, August 2d and August 15th. She grew progressively worse. On September 6th all symptoms were much aggravated. September 16th diarrhœa

seems to have improved; the skin was better, the mouth was better; she was decidedly weaker. This patient grew steadily worse, the skin symptoms spreading and the mouth getting into very bad condition until other treatment was instituted, to which she apparently reacted. On September 26th, 1912, the symptoms had apparently cleared up, but she was growing weaker and was expected to die.

THE NEW SERUM TREATMENT OF PELLAGRA.

By W. C. BROWNSON, Asheville, N. C.

The recently published paper of Dr. Jean Nicolaidi describes the results of experiments made by him with an "organo-mineralized radio-activated serum" that he devised for the treatment of pellagra. Dr. Nicolaidi found that in this disease certain important constituents of the blood are greatly diminished. The blood is "demineralized," as he expresses it. He, believing that this lack could be supplied by a serum containing the elements required by the impoverished blood, after much experimentation, succeeded in his efforts "to unite all the elements extracted from horse serum by evaporation in a vacuum which he treated subsequently by means of a solution saturated with carbonic acid containing all the organic and mineral salts of the blood plasma." Then, to increase its efficacy, he decided to render the liquid radio-active. By what process the serum was endowed with radio-activity he does not inform us beyond saying that it was "by a special process of great efficiency."

Dr. Nicolaidi used the serum first in Roumania, and in 1909 and 1910 treated fifty cases there with the most gratifying results. The serum is used intra-muscularly or hypodermatically in the buttock or flank in an average dose of 50 cc. for an adult. It is given, as a rule, every other day if the injection does not cause too much irritation. (Some pain is expected, and vaso-motor symptoms sometimes follow.) The course of treatment is completed by twenty or twenty-five injections.

In Dr. Nicolaidi's article he speaks particularly of the experiments made with his serum in Udine, Italy, in September and October, 1911. In consequence of the favorable results attained in Roumania, the treatment was brought to the knowledge of the Italian government, and Dr. Nicolaidi was requested to undertake the treatment of a series of cases in that country. A detailed account of these experiments is given in the Rivista Pellagrologica Italiana for November, 1911. The Rivista is a bimonthly journal published at Udine by the permanent committee of the International League Against Pellagra. Full case histories are given in this November number, and an exhaustive analysis of the urine of every patient

under observation before and during treatment is a feature of the report.

There are some discrepancies between the Italian report of the experiments and Dr. Nicolaidi's account of the test to which it may be well to call your attention.

"The cases chosen for these experiments (Dr. Nicolaidi says) were all in a most advanced state in spite of all treatments tried during long months. No satisfactory result could be obtained in these patients."

The cases were all in an advanced state, so far as chronicity is concerned, no acute cases being mentioned in the Rivista report; that is, none beginning that year. One was a second year case, the disease having appeared first in June, 1910. Then we have them of two, five, ten, even thirty or forty years' duration. Still there were none that we here in America would call especially grave, not even cases seven and nine, which are copied in full by Dr. Nicolaidi from the Rivista article. There is no evidence that they have been especially unresponsive to ordinary measures of treatment adopted in former years unless it be in cases seven and nine described. There had simply been annual exacerbations which subsided after a time.

We are told by Dr. Nicolaidi that all of the cases subjected to the serum treatment had "profuse diarrhœa (five to thirty stools a day)," "vomitings," "extreme agitation," "access of frenzy," "imbecility," "impossibility to stand alone," "intense cachexy."

The report of Drs. Grillo and Maj in the Rivista fails to show that the patients exhibited such alarming symptoms. Only in the two cases cited by Dr. Nicolaidi was the diarrhœa profuse. Some had no diarrhœa at all. In some it was slight. And one looks in vain even in the American article for the "constant pyrosis," "inability to stand alone," "intense cachexy," etc.

Dr. Nicolaidi speaks of the "numerous cases" treated at Udine. The cases numbered twelve in all. Nine were treated at the "local sanitarium," three at the insane asylum.

Of the first nine, all improved, some of them very markedly. All gained weight, all felt increased force, some were eager to go to work. How much of this improvement was due to better feeding, careful nursing, and improved surroundings we cannot say. Some credit should be given these agencies certainly. Then the cooler

season coming on during the treatment also counts for something. There must have been great virtue in the serum undoubtedly, the cases uniformly responding speedily to the injections by diminished gastrointestinal irritation and a general sense of well-being.

In the three asylum cases the outcome was disappointing, but one improved. One remained unimproved; one died. This last case, it is but just to add, was a mixed infection, the patient being a heavy drinker with profuse diarrhœa and delirium tremens.

It is said "the patient appeared to show some improvement from the injections of serum, but died from collapse."

Dr. Antonini, who writes a foreword in the Rivista to the detailed account presented by Drs. Grillo and Maj, who supervised Dr. Nicolaidi's work, is not correctly quoted by Dr. Nicolaidi. One would gain the impression from the article in The Southern Medical Journal for August that Dr. Antonini regarded the serum as a *cure* for pellagra; but in closing his introduction what he does say is, "If we are not in certain possession of the specific that will of itself cause pellagra to disappear, we have attained an excellent aid in the struggle against the disease when there is need of active intervention."

Again Dr. Nicolaidi fails to give the final words in the summing up of Drs. Grillo and Maj. These are, "Can we say that the disease is cured in those cases which we assist to a decisive improvement of nutrition and of force? We know by experience that no disease offers such grave and unexpected relapses as pellagra, and whatever its pathogenesis may prove to be, we are still convinced that it is a chronic malady. We must, then, verify the good symptomatic results of the treatment and await new experiments and observations on these same cases. We reserve for a further communication information as to the efficacy of the treatment as shown hereafter."

It should be distinctly understood that I am not opposing the serum; no one could read the Rivista article without being impressed by the rapid improvement in the cases under treatment. I would be most happy to use the serum were a supply available, and with high hopes of benefiting my patients thereby. I simply wish to correct any misapprehensions that may have arisen from Dr. Nicolaidi's article, and warn against any possible exploitation of the serum as a "sure cure" for pellagra.

No further report of these cases has appeared in print. Drs. Grillo and Maj have forwarded a paper to this conference giving "Later Results on Pellagrins Subjected to Nicolaidi's Serum Therapy in 1911," which Dr. Babcock kindly allowed me to read. Numbers seven and nine, discribed in Dr. Nicolaidi's paper, are said to be in excellent condition this year, with no sign of recurrence. One (No. 6) had a "grave recidive this year to which she succumbed." Five others have shown slight evidences of the old trouble, it appears, but with one exception have been able to continue at work.

Drs. Grillo and Maj consider the results satisfactory, and they conclude by saying, "We can affirm * * * that Nicolaidi's serotherapy is a treatment of high efficacy in the cure of pellagra."

It is quite possible you may not share their opinion.

VII. Miscellaneous Aspects of Pellagra

MEDICO-LEGAL RELATIONS OF PELLAGRA.

By J. W. Babcock, M. D., Physician and Superintendent, State Hospital for the Insane, Columbia, S. C.

The general parallelism to be found in the history of pellagra in the Old and the New World, although striking, is perhaps after all merely corroborative evidence of the clinical identity of the disease as found in both hemispheres. In no respect is this historical and clinical similarity more marked than in the little studied though highly important medico-legal relations of pellagra.

European.—To Legrand du Saulle,[1] of France, seems to belong the honor of having first directed attention to the importance of this aspect of the malady. He emphasized the fact that from the medico-legal point of view the most salient phenomena of pellagra consist in vertiginous crises, in acts of violence, and in irresistible impulses to homicide and suicide. Following up the study of the jurisprudence of pellagra in 1865, Sorbets[2] wrote: "This is a question which calls for the investigations of all physicians living in countries where they meet with cases of pellagra." It was doubtless a painful confession for the distinguished Landouzy to make when he said: "I have since been convinced that I once allowed to be executed for homicide a woman, who, without doubt, had committed the deed during an attack of pellagrous insanity." After his life-long experience with the disease, and with the insane, Lombroso left the opinion that "A common symptom of pellagra is the tendency to unpremeditated murder or suicide without the slightest cause. The sight of water suggests drowning in the form of murder or suicide." Or as Marie[3] says: "Suicides by drowning are numerous also by reason of a kind of motor automatism or instinctive impulsion similar to attacks in epileptics. They do not know when they throw themselves into the water, and if they survive they cannot explain their attempt." This "hydromania" of Strambio, that is, the impulse of pellagrins to drown themselves, has been discussed by all writers upon the disease since his time (*circa* 1785). Sorbets,[2] however,

takes a more comprehensive view of the subject in asserting that "Nothing is more capricious or variable than pellagrous insanity. Almost all pellagrins experience a special *penchant* to drown themselves, although others perish by strangulation, or throw themselves from high places, or, according to Soler, into the fire." And he adds: "But it is not only against themselves that pellagrins direct their insane acts; under the influence of homicidal monomania they have other victims. Thus, then, pellagra is a malady in which, at an undetermined stage, the intellectual faculties are obliterated, abolished or obtunded. The patient does not properly judge his condition, his position, or his relationship to his environment; he commits the most reprehensible acts without motives, and this is the most convincing proof of his insanity. One who commits murder from personal interest, for robbery or from revenge, is not in the same category as one who commits homicide because of an accidental derangement of his mental faculties, and without an interested motive. This is the fundamental principle of all legislation which excuses the acts of the insane. * * * Thus pellagrins, who are attacked by well established pellagrous insanity * * * have obeyed a power, a force which they cannot resist, and, hence, do not come under the penalty of the law. This is the point of view which it is necessary to recognize regarding this grave question, which concerns the dignity of families, and the honor of justice." To this may be added the opinion by du Saulle[1]: "Pellagrins, for example, who obey homicidal impulses, which so frequently accompany their insanity, have been condemned as murderers, and this with the consent of medical experts, or at least it is in accordance with the conclusions of their reports, that these unjust sentences have been pronounced."

Antonini,[4] the Italian alienist and pellagrologist, has written that: "In pellagrous regions there are frequent cases in which it is possible to find in indicted persons some outward expression of pellagra, even when the examination is made some time after the actual deed or during the progress of the trial. * * * To the expert alienist it will not be difficult to establish his case in persons suffering from severe pellagra. Usually these facts will have been recorded by the examining physician who has sent the patient to an insane asylum. But pellagra may be present in an able-bodied farmer who has not felt the need of medical advice."

Legrand du Saulle[1] has suggested as a method of inquiry that "In examining a criminal suspected of pellagra, the expert would naturally inquire whether the act committed presented any relation to the delirious manifestations, hallucinations and impulses which are ordinarily observed in this affection; if he has been able to find it under the direct dependence of maniacal excitement, stuporous depression or dementia, the three common forms of pellagrous insanity; if it were done at the time of vernal exacerbations; if insolation was an etiologic circumstance; if the tongue shows signs of a gastric involvement; if the hands present the pathognomonic erythema; if vertigo preceded for several days; if he shows locomotor vacillation; and if previous suicidal attempts have been made as shown by cicatrices."

Mongeri,[5] another Italian authority, has summed up his views upon the responsibility of pellagrins in these words: "The legal measures, civil and criminal, which a magistrate ought to apply, and the expert request for the benefit of pellagrins are various: while a pellagrin is in the early erythematous stage, it is not possible to raise in a court of justice the question of his enjoying the full use of his mental faculties; therefore, it would be difficult for one to appeal for an attenuation of punishment for an alleged criminal upon the single fact that he has the pellagrous erythema. When, however, the disease-process has become complete, and mental disturbance is added to the physical phenomena, one would be obliged to appeal for a stay of proceedings in a court of justice, and absolute irresponsibility in an institution because there are moments when the pellagrin so completely loses his power of self-control as no longer to be able to restrain himself from doing a criminal act."

But Legrande du Saulle[1] directed attention to an unusual evolution of pellagrous insanity by asserting that "Although mental alienation is usually a late manifestation in cases of pellagra, it sometimes precedes the development of gastro-intestinal and cutaneous symptoms. Two such cases were noted by Strambio and one by Landouzy."

Civil Capacity.—Sorbets[2] reached the conclusion that: "Examined from the point of view of the civil consequences, pellagra is a great peril. After what has been said of the nature of the insanity, one may easily divine that the isolation, the melancholy depression, and the ideas of persecution can undermine at any time the free will

of a donor, or the capacity of a testator, or give opportunity for the base intrigues of adventurers."

Diagnosis.—As noted by Lombroso, and quoted by Marie[3]: "Frequently the pellagrous psychosis appears under the form of a special melancholia, more often in the form of an insanity with systematized delusions. This last form may be observed in hereditary pellagra; vagaries of memory, self-accusations, nosophobia, apprehensions of personal violence, delusions of pregnancy, loss of personality, and concealment of sex, have all been noted.

"A woman of Seronno, 38 years old, confided mysteriously to the judge that she had been violated, and had become pregnant. She believed that she had given birth to a child, and then, with the help of her seducer, had buried it alive; for three months she led the officers of justice to many places in search of the little corpse; when finally a medical examination revealed that she was a virgin suffering from pellagra." Sorbets[2] affirms: "For alienists, hallucinations are the chief characteristic, the pathogomonic phenomenon of pellagrous insanity."

It was the opinion of Legrand du Saulle[1] that pellagrous insanity cannot be simulated with any degree of success by virtue of the multiplicity of the phenomena which it assumes from time to time. From his researches upon the subject, du Saulle advanced these propositions: 1. In pellagrins, whose intelligence has become affected, the insanity often undergoes transformations, but impulses to homicide and to suicide persist, and aid in clearing up the medico-legal diagnosis. 2. Psychic disturbances precede in some cases the alterations of nutrition and the cutaneous phenomena, and this circumstance, especially, if pellagra is sporadic, exposes the medico-legal expert to grave errors, which examination extended over a considerable time can alone enable him to avoid. 3. Pellagrous insanity well verified establishes in criminal procedure irresponsibility for the acts committed, and in civil cases the just suspicion of agreements, contracts, benefactions and wills.

Among the crimes recorded in Europe., as committed by pellagrins, are suicide, homicide, infanticide (Alpago-Nevello[8]), cleptomania (Tamburini[9]) and false accusation. Reference has just been made to some of the civil cases that may arise in connection with the disease.

To sum up we may quote Sorbets:[2] "Well established pellagrous insanity implies in criminal law irresponsibility for the acts committed, and in civil law raises the just suspicion of sales, contracts, donations and wills."

Egyptian.—Dr. John Warnock,[6] Director of the Government Hospital for the Insane near Cairo, reported in 1903: Fifty-two patients suffering from pellagrous insanity were admitted, of whom seven were criminal lunatics. Delusions of persecution, of being put under a spell, or of being poisoned, etc., are frequent mental symptoms of this malady, and it is therefore not surprising to find that five murders were committed by these patients before being sent to the asylum as criminal lunatics. In 1902, also, two murders committed by men suffering from pellagra occurred to my knowledge. These patients are very prone to suicide and to injure their children. It is to be regretted that so many of them have to be sent back to their homes before recovery, especially as prolonged treatment would appear to cure a certain proportion of cases."

Sandwith,[7] from his experience with pellagra in Egypt, has noted "That many criminal lunatics, brought to the Cairo Asylum, are found to be pellagrous; they have been arrested for some purposeless murder in consequence of delusions which they forget and deny a few days after admission. One such case was said by his family to be quiet generally, but to have violent outbreaks every winter. He remained melancholic but quiet at the asylum for eleven months, and then suddenly (in January, 1904) attacked another patient without warning, and would have killed him if the attendants had not interfered; his excuse was that the man was beginning to persecute him."

American.—So far as I have been able to learn, the medico-legal side of pellagra has hitherto not been discussed separately by American writers, although much activity has been shown regarding most of the other aspects of the disease. To show that the history of pellagra, in this respect also, has been repeated in our country, I beg leave to submit a number of brief outlines of cases compiled from newspaper reports from many parts of the United States, as well as from medical journals and selected from personal experience:

At the July, 1913, term of court in Chester, S. C., the jury brought in the verdict of "Not guilty of murder on account of insanity" in the case of The State *v.* Richard R. Reighley, who had killed Free-

man A. Wright several months previously. The attorneys for the defense showed that the accused was suffering from insanity attributed to pellagra. The solicitor (prosecuting attorney) accepted the evidence of Dr. H. E. McConnell upon this point. The manuscript of this paper was also used and quoted by the attorneys at the trial. Reighley was acquitted as stated above. He was subsequently committed to the State Hospital for the Insane by the presiding judge and found to be a confirmed pellagrin.

I have notes of another case of homicide by a white woman, who, in November, 1909, it was alleged, shot the postmaster of a middle western town without warning, while suffering from melancholia "brought on by rheumatism and pellagra." The records of the court, however, do not establish the presence of pellagra in the case, nor was it referred to by the defense. The patient was placed in an asylum.

Near Grayson, La., September 9, 1913, Mrs. R. S., in the last stages of pellagra, was reported to have become insane and to have made several ineffectual attempts upon the lives of her children, as well as upon her own life. Although regarded as a constant menace to her family, in view of the fact that she appeared to have only a short time to live, her friends decided to watch her and not commit her to an asylum.

Suicides by pellagrins have frequently been reported by the newspapers. These reports usually employ such adjectives as "dread," "incurable," *et cetera*, and no doubt, as has been claimed, contribute to the development of the pellagraphobia, which is widespread in some parts of the country. While I confess that the presentation of the notes on these cases forms a chapter of horrors, yet taken together they make a part of the early history of pellagra in the United States and, therefore, are worthy of record. They also serve to emphasize the peculiar relationship which the malady sometimes bears to the body politic.

Mr. T. E., of Lancaster, S. C., 53 years old, a pellagrous mill operative, committed suicide in August, 1911, by drowning in a pond near the mills. His rescue was attempted, but E. refused help, and saying, "I am going to drown," threw himself again into deep water and disappeared. E. was in the last stage of pellagra, and, upon the recovery of his body, it was found that his clothing was weighted with stone, thus indicating premeditation. Despondent because of

continued suffering with pellagra, Mrs. M. C., of Spartanburg, S. C., committed suicide by drowning in a pond August, 1912. I know of three other suicides of pellagrins by drowning in ponds in South Carolina. At Columbia, S. C., April 26, 1914, Mrs. J. L. T., a pellagrin, was found dead in a bath-tub in her home at 6 a. m. The cause of her death was given by the coroner as drowning and the contributory cause as pellagra. Miss K. T., of Cross Keys, Ga., ended her life June 5, 1913, by jumping into a well. "She was a victim of the dreaded pellagra." She left a note saying: "I have decided to end my suffering by seeking death. You will find my body in the well next door." The "hydromania" of Strambio would thus appear to prevail in this country as it does in Italy. In the "pellagra belt,"—if there be any limitation to the widespread prevalence of the disease—it would, therefore, be well to consider this malady as a possible cause in cases of "inexplicable" drowning. In insane asylums both white and colored pellagrins, especially the women, are prone to attempt suicide by drowning in bath-tubs.

I have notes of a female pellagrin, Mrs. X., a surgical patient in a general hospital at the same time with her baby who had "marasmus." Being on a different ward from her child, she worried a great deal over the separation, became noisy day and night and finally developed the homesickness so characteristic of pellagra. She was frequently detected by the nurses filling the ward bath-tub and turning on the gas. Because of these tendencies she required constant watching, but she was finally taken home before the occurrence of a serious accident. Her subsequent history is not known to me.

Other methods of suicide by pellagrins have also been reported. Among these may be mentioned: That of Mr. M. K., of Society Hill, S. C., in October, 1910, by hanging; of Mrs. C., of Tennessee, July, 1911, by carbolic acid; of Mrs. B., of Wiggins, Miss., who, having had pellagra 18 months, became suddenly insane in September, 1910, and tried to commit suicide; of Mrs. J. H. M., of Gainesville, Ga., who, in October, 1910, becoming despondent because she believed she would never recover from pellagra, committed suicide; of Mrs. E. H., of Greenwood, S. C., a pellagrin, who, in October, 1910, attempted suicide by slashing her throat with a pocketknife. In August, 1911, Mr. T. B. B., 53 years old, a respected citizen of Birmingham, Ala., and a pellagrin, cut his throat with a razor. Desperate and insane as a result of pellagra, W. A. G., of Durham,

N. C., October, 1911, shot himself in the head with fatal result. At Milledgeville, Ga., in March, 1912, A. W., aged 72 years, an insane pellagra patient under private care, threw himself under a freight train and was instantly killed. The attendant in charge of him attempted to pull him from the track, but W. held on tightly to the rail and was beheaded.

In November, 1912, Mrs. J. P., of Columbus, Ga., aged 30 years, having been mentally deranged from pellagra for some time, committed suicide by stabbing herself in the left breast with a pocket-knife. She had previously made two or three unsuccessful attempts upon her life, and, although closely watched, she finally succeeded with a knife she had borrowed to peel an orange. At Stantonsburg, N. C., in November, 1912, W. J. E., 35 years old, a well known citizen, having been ill for several years with pellagra, killed himself by drinking wood alcohol. It is supposed he had grown despondent over his condition and committed the act impulsively during the brief absence of his wife. In June, 1913, Mary G., colored, and a pellagrin, whose mind had been slightly impaired for some time, after writing directions concerning her five children, committed suicide by hanging. This is the more noteworthy as suicide among the colored race is comparatively rare. I have records of a negro man "who beat his brains out against the wall of his house," the cause assigned for his act being pellagra. In April, 1913, it was reported from Wichita Falls, Texas, that R. N. M., a retired farmer, 52 years old, and a sufferer from pellagra for some time, was found dead in his barn with two bullet holes in his breast. He left a note addressed to his wife saying he thought he was acting for the best. Mr. W. M. M., a carpenter, aged 52 years, committed suicide by drinking carbolic acid at Spartanburg, S. C., November 14, 1913. He had been ill with pellagra for a year. Despondent over his inability to work at his trade he ended his life in the temporary absence of his daughter, with whom he was living. These citations from newspaper accounts show the frequency of these tragedies arising from pellagra among the general population. Aside from their medico-legal value, may they not serve also to put physicians on their guard for symptoms of depression when treating pellagrins?

I have also known of an alienated white female pellagrin committing suicide by hanging herself from a window grating by her own hair, and a few strands of twine which she had concealed.[10] A white

female pellagrin in a general hospital, while depressed over her condition, which she regarded as hopeless, drank, with suicidal intent, a quantity of alcohol which she seized from a nurse's basket. Soon after her removal home, she drank a half pint of whiskey, and two ounces of tincture of nux vomica with the same object. Later she ran away from home at night, and was found lying in a shallow pool of water in the road. These acts necessitated her confinement in an institution. Her asylum residence lasted about eight months, and was marked by frequent suicidal attempts. She gradually improved; and, having partially recovered, was finally taken home against advice. It is rumored that she is now well.

The obsession for self-destruction is thus shown to be very common with pellagrins in this country, and while we must recognize their strong inclination to drown themselves (the "hydromania" of Strambio), in view of the many other methods of suicide to which they resort and of their homicidal tendencies it might be well to adopt the single term of thanatophilia as applying to the compulsion for ending life, which so often dominates their will and conduct.

In September, 1912, I saw an interesting case of self-mutilation in a white male pellagrin, who was insane: E. T. B., 35 years old, having had pellagra five years, and having been in an asylum about two months, suddenly bit off the tip of his tongue and the tip of the index finger of the left hand nearly up to the base of the nail, and tore off the nails of the little and ring fingers of the right hand. Usually mute and always reticent, he, after much persuasion, explained the reason for his act, by saying, "I did it because I could not help it."

Another case illustrating compulsions is that of Mrs. A. B. B., 42 years of age, admitted to our State Hospital September 5, 1913. She had been in failing health since the previous January. Although pellagra was not suspected, for several months her conduct had been such that she had to be watched. She once aroused her husband at night, saying: "Wake up and let me tell you what I was trying to do; when I came to myself I was trying to get the oil-can to burn the house." In August she attempted to throw herself from a window of a tall building, and on being rescued said: "Just let me alone, I am crazy." On being taken home she deplored her actions, and did not appear confused. Upon admission to the hospital, examination disclosed rough skin on the backs of her hands

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and fingers. The mucosa of her mouth was fiery red, the tongue denuded, and there was decided salivation. She acknowledged that she had pulled out her eyebrows and complained of constipation and loss of appetite. Under treatment she improved rapidly, having gained 43 pounds when she was taken home, October 11, 1913. about five weeks after admission.

Dr. Eleanora B. Saunders, while woman physician at the South Carolina State Hospital, reported[10] a case of medico-legal interest, which, in brief, is that of Mrs. P., 33 years old, with mental aberration appearing late after an attack of pellagra in 1910 Among other symptoms the patient imagined herself pregnant and had a uterine "crisis," lasting three hours, the pains, to an observer, being typical of labor. For some weeks afterwards she insisted that she had been delivered of a child, and expressed great anxiety for its safety, accusing the physicians of cruelty in removing and concealing it from her. These delusions of pregnancy are not unusual among insane pellagrins, suffering from uterine and perineal lacerations. This fact is brought out here to show, in connection with Lombroso's case cited above of the woman of Seronno, that pellagrins with such delusions are especially prone to make false accusations, both against themselves and others. Obviously the modern conception of pathological liars—pseudologia phantastica—is suggested and should also be considered here.

Dr. D. M. Crosson, of Leesville, S. C., has given me this personal communication of the history of a pellagrin who has been under his observation for some time. Mrs. M. R. P., 45 years of age, the mother of six children, the youngest being now ten years old, has had pellagra for four years. Latterly she has developed the delusion that she is about to be confined. Influenced by this idea, within the past year she has summoned her physician six or seven times. She appears to be having labor-pains and asks to be delivered. Examination discloses absence of pregnancy. She has hemorrhoids but no pelvic lacerations. No other delusions were discovered.

At Nashville, Tenn., in November, 1911, J. F. W. and wife filed a bill in the chancery court against H. H. R., praying that an exchange of land for notes be declared void and that the transfer be set aside because the plaintiff was a sufferer from pellagra at the time of the transaction, and was not of sufficient soundness, mentally, to protect himself in the trade. Under date of September 18, 1912, I was

informed by Robert Vaughn, Esq., clerk and master of the chancery court at Nashville, that "From an inspection of the depositions in the case of W. *v.* R. I see that two physicians were introduced, who stated in a general way that patients suffering with pellagra in addition to marks upon the hands and other portions of the body, which are characteristic of the disease, also had bowel trouble and frequently the mind became involved or impaired. The cause has not been tried yet by the court, hence there has been no decision as to what extent, if at all, the complainant, W's., mind was affected by pellagra." On March 31, 1913, this case was still on the docket, having never been heard or disposed of.

Instances are known of asylums in which the diagnosis of pellagra having been overlooked, nurses have been unjustly discharged for alleged neglect in bathing patients, the pellagrous erythema being mistaken for burns and scalds. In doubtful cases of this nature pellagra should be considered as a possibility.

Dr. J. J. Watson, of Columbia, S. C., thinks a large proportion, probably 90%, of the pellagrins he has had under care in a general hospital prevaricate or fabricate. Especially is this noticeable in their complaints against nurses for alleged omissions of the treatment ordered or for improperly carrying out the physician's directions. Investigation has proven all such charges and suspicions to be without foundation. Sometimes this mental attitude of pellagrins suggests the fabrication of Korsakoff's Syndrome. The hysterical character is also suggested. It seems to arise either from amnesia or else from hallucinations. It obviously is not due to a desire to make mischief.

The liability of pellagrins seemingly convalescent to sudden death, deserves to be brought to the attention of medical examiners and coroners. A similar tendency has been noted in beri-beri. In pellagra these attacks may simulate angina pectoris.

Naturally, the question arises: To what extent are these criminal, abnormal or unusual tendencies due to pellagra *per se,* and to what extent do they belong to insanity in general? I shall not undertake to answer this question narrowly. In many of the cases cited the two conditions of pellagra and insanity have been coexistent, and in most of them the insanity appears to have followed the pellagra. The inter-relationship of the two conditions is a separate question, and properly does not belong here. My own opinion is that the

several acts described in this paper have arisen from a mental condition due to the pellagrous intoxication, which has either greatly modified or nullified individual responsibility.

The cases cited here have occurred in eight States—North Carolina, South Carolina, Georgia, Tennessee, Alabama, Mississippi, Louisiana, and Texas—and they necessarily must constitute but a small proportion of those actually occurring in this territory and in this country in the last three or four years, and associated with pellagra, since they have been compiled by a single student of the subject. But collectively they demonstrate the variety of abnormal actions which have been attributable to the unknown poison of pellagra. Furthermore, these actions duplicate, in a general way, those reported by foreign observers.

It thus appears that evidence is slowly accumulating which goes to prove that the history of pellagra is being repeated in the United States and that among other burning questions which its discovery has aroused that of the medical jurisprudence of the disease is one with which the general practitioner, the neurologist, the alienist and the jurist will have to reckon. Certainly, as Sorbets[2] said: "This is a question which calls for the investigations of all physicians living in countries where they meet with cases of pellagra."

In conclusion, I quote again from Sorbets[2]: "From the medico-legal point of view, pellagra, as one sees it, raises a grave question which touches the highest interests of society, of ethics and of justice—interests which are most dear to man: the life of citizens and the honor of families. This question, first introduced by Legrand du Saulle, has not received the attention it deserves, but it is really a subject of great importance." It is to impress the "great importance" of this phase of pellagra upon American students of the disease at this comparatively early stage of our researches upon the malady that this paper has been prepared.

ACKNOWLEDGMENT.

My thanks are especially due to Surgeon C. H. Lavinder, U. S. Public Health Service, for the privilege of consulting the valuable press clippings on pellagra, collected by his Bureau, without which the preparation and presentation of the American side of this question would have been impossible. For many favors I have again to record my gratitude to the officers of the Library, S. G. O., Army Medical Museum, Washington, D. C.

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DENTAL FINDINGS IN INSANE PELLAGRINS.

By S. F. KILLINGSWORTH, D. D. S., Dentist, State Hospital for the Insane, Columbia, S. C.

It seems to be generally admitted that pellagrins have usually suffered from other diseases before developing pellagra. In other words, pellagra is usually ingrafted upon a pre-existing cachexia. It cannot, therefore, be expected that such persons would have sound teeth. Furthermore, the teeth of the insane in my experience are very much neglected, and, therefore, in much worse condition than those of the sane. At this time I have no statistics on the subject for comparison between the teeth of the sane and insane, as I am reporting on insane pellagrins only.

It was Sandwith's observation in Egypt that "by far the greatest number of pellagrous patients have excellent teeth and perfect powers of mastication." These views have been corroborated in this country by Roberts, who says: "The teeth are not affected. In one series out of 166 pellagrins 120 had sound teeth. Pellagrins can usually masticate well and with them the teeth do not in any way influence the gastro-intestinal condition."

Zlatarovic has reported from his observation on the pellagrous patients at the government asylum at Pergine, Southern Tryol, Austria: "In almost 60 per cent. of our patients we could observe decided or complete and premature defectiveness of the teeth (due to tropic disturbances?)."

It having come within the line of my service to examine the teeth of the pellagrins in the South Carolina State Hospital for the Insane, I wish to put on record the findings of these cases.

WHITE FEMALES.—I examined twenty-one white women and found that only eight had good teeth and healthy gums; two were wearing full plates; six had gingivitis and stomatitis, and five had severe cases of pyorrhea alveolaris. In the above number there were three children with good teeth. They were under twelve years of age and one was under eight, with eight temporary teeth, all sound.

WHITE MALES.—I examined ten white men and found only four had good teeth, and there were some teeth missing in each of their mouths. Three had stomatitis and three with pyorrhea alveolaris.

COLORED FEMALES.—Of the twenty-one examined, I found eleven had good teeth; two had pyorrhea alveolaris; ten had ulcerative stomatitis, which seems to have been caused by general ill health, as the patients showed signs of having been affected for a long time.

Summing up the above findings, out of the fifty-two pellagrous patients examined, twenty-one had good teeth; ten had pronounced cases of pyorrhea alveolaris; two wore plates, and nineteen had ginibitis and stomatitis, making the percentage of those with bad or unsound teeth 60 per cent. Of the number examined fully 20 per cent. had pyorrhea alveolaris.

SALIVA.—I found the saliva in 80 per cent. of the patients acid; 10 per cent. neutral, and 10 per cent. normal, that is, alkaline.

I had hoped to go further into this investigation, but the opportunity has been denied me.

THE SOCIOLOGICAL ASPECT OF PELLAGRA.

By L. B. MYERS. Charlotte, N. C., General Secretary The Associated Charities.

The preacher, the teacher, the doctor, the social worker have been drawn close together in recent years in the great work of saving humanity from the overwhelming load of miseries that for centuries have borne it down. They are beginning to recognize each other not as of separate and distinct professions, but as of different branches of one great profession—that of saving men and women to become happy and efficient units of society. There is a call of humanity for better team work among these four branches of the great profession that Jesus of Nazareth followed—that of saving men. This co-operation or team work has been much in evidence in the cure of tuberculosis. A beginning has been made in the treatment of some other diseases. Certainly such co-operation is necessary in all diseases that are apt to run a long term, and pellagra belongs to this class.

A case of pellagra frequently constitutes a social problem fully as serious as the medical problem is grave. This is the more especially so if it is the bread winner, the father of the family, or the mother who is stricken. The often long-continued term of the disease, the fluctuating severity, the uncertainty of the outcome, the, perhaps, ill-founded fear of contagion, the inadvisability of the patient returning to work until completely recovered, all add to the difficulties of the social problem. All the social problems are more acute among the poor, and pellagra is most often found in this class. The loss to society in wages unearned, in families poorly fed, in children kept from school and in the care of widows and orphans can only be conjectured, but is very large. Any propaganda, no matter how costly, for education or research that lessens the grip of this disease will save for the people many times its cost each year.

The problem of charity or relief of the poor is strictly a social problem, and as such comes into direct contact with pellagra. Next to tuberculosis, pellagra is the most difficult disease the organized charity worker has to deal with. Often for months, and sometimes for years, the entire income of the family is cut off while the presence of the sick man makes impossible that readjustment of the

family which might be easily accomplished in the event of his death. Long continued illness is a much more difficult social problem than death.

The study of the family resources, the adjustment of the family to its reduced income, and the development of an earning capacity in the members of the family who never before were wage-earners, all these, and a score more things that result therefrom, are beyond the doctor's power. Unless the family has character enough to accomplish this unaided, it must be done by the social worker in co-operation with the medical adviser. All the social resources of the community may need to be called into co-operation.

After a patient's partial or complete recovery, we have confronting us the problem of getting him reinstated into industrial life. Where a man of the unambitious class has been idle for a year or more, it is often difficult to get him back to work. It is notorious that in saving the lives of men and women, or children, we often ruin them, as far as world usefulness is concerned. It is this that makes it so important to find employment for the partially disabled and the convalescents from diseases that run a long term. For what does it profit a man to save his body if in doing this we ruin his soul? Instances are numerous where the life of a husband has been saved by great sacrifice on the part of the wife and children, only to have that husband and father spend the rest of his days in idleness, living off of the earnings of the same long-suffering wife and children. It is not the habit, in this day, for the doctor to say that he has no interest in the patient's family—or no interest in what becomes of the man after his discharge—or to say that his duty has been performed if he saves the life of the man. The great doctors of the day are co-operating with social workers not only to save the man's life, but to save the man. It is this that is glorifying the work of the doctor and making him an accepted disciple of the Great Physician of David's line.

The cause of pellagra is not at this time determined, and we cannot speak positively as to means of prevention. But I am sure that whatever may finally be determined as the cause, whether spoiled grain, or the bite of an insect, or something else, its prevention will be to a large degree a social problem. The cause of tuberculosis is known and its cure is known, yet we are failing both to prevent and to cure it. Its cure and prevention is largely a

sociological problem and will require a social revolution. There must be a fundamental reformation of housing conditions among the poor and of living habits among one-half our population before we can hope to conquer the great white plague. As pellagra is most prevalent in the poorer social class, we have reason to believe that bad housing and drainage, unfavorable diet, poor cooking, filth, the presence of flies and mosquitoes, a polluted water supply, and other social ills are favorable to the disease, though not proved responsible for it. Improvement in these lines will in all probability reduce the number of cases in any locality, and a social revolution may be required for its final eradication.

If in the treatment of the disease a special diet is prescribed, the social problem again comes to the front. Is the family income sufficient to provide the diet? Is the housekeeper competent to prepare it properly, and are ordinary sanitary precautions observed, etc.?

It seems to me that the medical and social problems are so interwoven that wherever possible the doctor should call on the district nurse, settlement worker, organized charity worker, or other social agency to co-operate with him in the task of saving the patient and his family.

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